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Appendix to the

DIABETES MELLITUS COORDINATING COMMITTEE

Sixth Annual Report to the Director National Institutes of Health Fiscal Year 1979

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health

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DIABETES MELLITUS COORDINATING COMMITTEE

Sixth Annual Report to the Director
National Institutes of Health
Fiscal Year 1979

NIH Publication No. 80-2243

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health

Public Law 93-354
National Diabetes Mellitus Research and Education Act

Sec. 5 (a) Part D of Title IV of the Public Health Service Act is amended by adding at the end thereof the following new section:

Diabetes Mellitus Coordinating Committee

"Sec. 436. For the purpose of —

"(1) better coordination of the total National Institutes of Health research activities relating to diabetes mellitus and

"(2) coordinating those aspects of all Federal health programs and activities relating to diabetes mellitus to assure the adequacy and technical soundness of such programs and activities and to provide for the full communication and exchange of information necessary to maintain adequate coordination of such programs and activities,

the Director of the National Institutes of Health shall establish a Diabetes Mellitus Coordinating Committee. The Committee shall be composed of the Directors (or their designated representatives) of each of the Institutes and divisions involved in diabetes-related research and shall include representation from all Federal departments and agencies whose programs involve health functions or responsibilities as determined by the Secretary. The Committee shall be chaired by the Director of the National Institutes of Health (or his designated representative). The Committee shall prepare a report as soon after the end of each fiscal year as possible for the Director of the National Institutes of Health detailing the work of the Committee in carrying out the coordinating activities described in paragraphs (1) and (2)."

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20205

Donald S. Fredrickson, M.D.
Director
National Institutes of Health
Bethesda, Maryland 20205

Dear Dr. Fredrickson:

I am submitting to you the sixth annual report of the Diabetes Mellitus Coordinating Committee (DMCC). This report, which is required by Public Law 93-354, describes all diabetes-related activities of the Federal government during FY 1979 and explains efforts to coordinate those activities. This year we have developed a new and more readable format for the report. This information is presented in two separate bindings. The body of the report is a narrative description and provides an overview of the DMCC, cooperative efforts of participating organizations, highlights of FY 1979 achievements, future plans, and summary tables presenting funding information on the various categories of FY 1979 Federal activities relevant to diabetes. An appendix, separately bound, lists all FY 1979 Federal projects related to diabetes by category of activity. It too presents summary tabular data and is intended for a specialized audience.

Although we are encouraged by the achievements of the past year, there remain many activities that could enhance efforts to solve the problems of diabetes. These activities span the range of Federal programs from basic research to efforts to improve the organization and delivery of health care services. All of the agencies participating in the DMCC are making special efforts to cooperate in meeting the needs for an intensified effort to address the many problems associated with diabetes. We hope that a continuation of these cooperative efforts will bring additional achievements in the years that lie ahead.

Sincerely,

Lester B. Salans, M.D.
Associate Director for Diabetes,
Endocrinology, and Metabolic Diseases
National Institute of Arthritis,
Metabolism, and Digestive Diseases
Chairman, Diabetes Mellitus
Coordinating Committee

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I. The Challenge
of Coordinating Diabetes Programs

Legislative Authority and Purpose

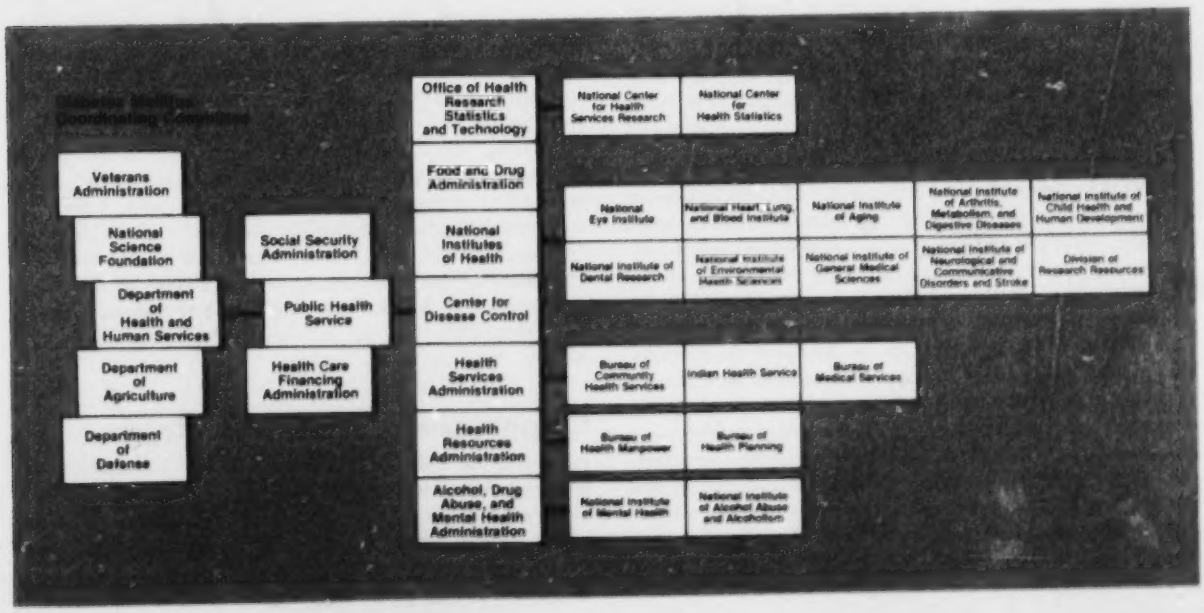
Recognizing the need for improved coordination of Federal diabetes activities, Congress mandated the establishment of the Diabetes Mellitus Coordinating Committee (DMCC) in 1974 (P.L. 93-354). The mission of the Committee was to improve Federal efforts to understand and control diabetes mellitus by improving the coordination of research and health care programs conducted by the National Institutes of Health (NIH) and other Federal departments and agencies. Since 1974, the DMCC has worked with first the National Commission on Diabetes and later the National Diabetes Advisory Board (NDAB) and many Federal programs to develop improved approaches to information exchange, joint planning, and the identification of promising areas for cooperative undertakings.

The DMCC includes representatives from 36 units of the Federal government, all of which are directly involved in the conduct or support of efforts to solve diabetes problems. The following figure indicates the Federal agencies and departments represented on the DMCC during FY 1979. This figure illustrates the diversity of organizational locations, interrelationships, and broad categories of endeavor with which the DMCC and this report are concerned. Though not always categorical in focus, Federal diabetes activities range from research support to direct provision of health care services, to a variety of health financing programs. Activities include educational efforts, from education for the patient to education for health care professionals and scientific investigators. Planning endeavors span the spectrum from the planning of health care facilities to the assessment of the needed direction in biomedical research. The conduct and sponsorship of research range from studies of improved methods of delivering and financing direct care, to clinical studies and investigations of fundamental disease processes at the cellular and even molecular levels.

Magnitude of the Problem

Diabetes mellitus is a serious and widespread disorder which affects Americans of all ages, backgrounds, and economic circumstances, although some groups, such as women, blacks, and American Indians, are more frequently affected. The toll the disorder exacts in early mortality, disability, sickness, daily attention, and suffering is considerable. It affects not only the patient, but also his family, close associates, and the community as a whole.

The exact causes of diabetes are not fully known, although the disease is characterized by elevated blood sugar and other metabolic disturbances. While appropriate management can control certain acute symptoms of diabetes, such complications as increased risk of kidney, heart, and blood vessel disease, and blindness are still a threat. These complications seriously impair the patient's quality of life and increase the risk of early death. The National Commission on Diabetes in its report has pointed out many of the problems associated with the disorder, and further statistics obtained from the National Diabetes Data Group attest to the severity of these problems:


Veterans Administration
National Science Foundation
Department of Health and Human Services
Department of Agriculture
Department of Defense
Social Security Administration
Public Health Service
Health Care Financing Administration
Office of Health Research Statistics and Technology
Food and Drug Administration
National Institutes of Health
Center for Disease Control
Health Services Administration
Health Resources Administration
Alcohol, Drug Abuse, and Mental Health Administration
National Center for Health Services Research
National Center for Health Statistics
National Eye Institute
National Heart, Lung, and Blood Institute
National Institute of Aging
National Institute of Arthritis, Metabolism, and Digestive Diseases
National Institute of Child Health and Human Development
National Institute of Dental Research
National Institute of Environmental Health Sciences
National Institute of General Medical Sciences
National Institute of Neurological and Communicative Disorders and Stroke
Division of Research Resources
Bureau of Community Health Services
Indian Health Service
Bureau of Medical Services
Bureau of Health Manpower
Bureau of Health Planning
National Institute of Mental Health
National Institute of Alcohol Abuse and Alcoholism

2 The Challenge

- Approximately 5 million Americans (2.3% of the population) are known to have diabetes. It is estimated that another 5 million people have undiagnosed diabetes. Among persons aged 45 to 64 years, the rate is 5 percent; in the over-65 age group, the rate is as high as 1 in every 12 persons.
- Diabetes is the fifth-ranking cause of death by disease, accounting for 35,000 deaths in 1976. It is a contributing factor in at least an additional 90,000 deaths each year.
- About 25 percent of diabetics are under treatment for heart disease, and diabetes is one of the four major risk factors for heart disease. About 60 percent of diabetics die of cardiovascular disease.
- Diabetes is the second leading cause of blindness. About 40 percent of all diabetics have retinal vascular signs and, if left untreated, 10 percent of this population can be expected to develop vision loss.
- Diabetes is the fourth leading cause of visits to general and family practice physicians. About 90 percent of diabetics see a physician at least once a year, and one-third of all diabetics see a physician five or more times each year. One-third of all diabetics have been hospitalized because of their disease.
- Approximately 500,000 women of childbearing age in the United States have diabetes. During pregnancy, even with the best of care, such women face a probability of neonatal death that is four times greater than that of nondiabetic women. The risk of the diabetic mother's child having congenital abnormalities is also greater, ranging from one to four times higher depending on the severity of the mother's condition.
- The direct and indirect costs of diabetes mellitus have been estimated between $6.8 billion and $20 billion annually (for 1977).

The NDAB, created by legislative action (P.L. 94-562) in response to a recommendation of the National Commission on Diabetes, monitors the progress of Federal programs in implementing the recommendations of the National Commission on Diabetes and modifies or makes new recommendations, reporting annually on the overall progress of diabetes efforts. Voluntary organizations, professional associations, patient advocacy groups, academic institutions, government programs, and private individuals have all been involved in a variety of attacks on diabetes. In many instances there is a long history of cooperation and communication, for example, the relationship between voluntary organizations and the National Institutes of Health. The magnitude and variety of these activities creates substantial needs for effective communication, careful coordination, and the development of cooperative approaches.

DMCC Approach

Since its initiation, the DMCC has identified specific areas and has taken practical steps to improve coordination. These efforts have often focused on improved communication and the development of necessary information resources. The five preceding reports of the DMCC all attest to the Committee's efforts to inventory and organize program information concerning the overall Federal effort in diabetes. Gradual refinement of reporting categories has greatly benefited the Federal sector in its ability to categorize diabetes research and nonresearch activities, and this classification, although still being refined, has assisted in identifying areas within which agencies may cooperate successfully. Based on the data collected by the Committee, it has become possible not only to identify the magnitude and nature of Federal diabetes activities, but also to identify all the agencies participating in a given area of endeavor, to identify gaps and duplications, and to uncover areas where joint approaches would be fruitful.

The Committee's examination of Federal activities and the overview and recommendations of the NDAB in a variety of areas have also led to direct action to improve program activities. Examples of recent cooperative undertakings are described in the next chapter. The DMCC information exchange has often helped in the initiation of these programs and other undertakings.

The interdisciplinary exchange of ideas is as important as any other function that the Committee performs, and it is often this aspect of the Committee's undertakings that is most productive and gratifying in both administrative and personal terms. Through the Committee, administrators, scientists, teachers, health planners, epidemiologists, clinicians, and other health professionals have the opportunity to discuss problems, realize their respective achievements, and share methods in an atmosphere of familiarity and cooperation. The Committee itself provides only the forum for these discussions; it is the individual participants along with other colleagues from their agencies who provide or make available the expertise and dedication which allow actual problem solving. In this regard, the Committee and compilers of this report must express thanks to the many representatives and their sponsoring organizations which are responsible for the achievements described in this report.

Organization of the DMCC Report

In compiling this FY 1979 report, the Committee has chosen to take a new approach, which it feels will afford the audience a more comprehensive and readable view of the many Federal contributions to the understanding, treatment, and prevention of diabetes. The report has been divided into two parts. The first of these is this narrative

report which describes Federal efforts, focusing on cooperative endeavors carried out during FY 1979, major achievements of the individual organizations, and plans for the future. Each organization's achievements are discussed in light of its respective mission. Future plans are discussed in light of the overall effort and progress in diabetes programs. A separate section presents summary tables and graphs describing the funding levels for all FY 1979 Federal activities related to diabetes. The summary is organized by category of activity and sponsoring organization. In some areas, particularly those outside research, a discrete funding level related to diabetes alone cannot be identified. Activities of this sort are described in the narrative. The second part is an appendix for specialized uses that lists individual projects funded by the Federal government through various organizations. The projects are organized by a variety of cross-cutting scientific issues or activity areas, and these include both research and nonresearch categories. Like the report, this appendix includes summary tables and graphs describing funding levels by category and sponsoring organization. This approach to describing the relationships among various activities parallels the approach of the Committee itself: to view the totality of Federal efforts and their interrelatedness.

The Committee hopes that this report will allow the reader to discern not only the complexity of the many undertakings and achievements, but also the overall scope and unification of Federal efforts to overcome diabetes.

II. Building Relationships
and Strengthening Cooperative Efforts

Introduction

One of the most encouraging outcomes of DMCC activities has been the establishment of new working relationships among the participating organizations. At the time of the Committee's initiation, some interdepartmental relationships were strong, while among other organizations there was little contact concerning diabetes program implementation.

The Director of the National Institutes of Health has designated diabetes as a trans-NIH issue and this administrative action has succeeded in unifying diabetes programs and establishing lead responsibility in the NIAMDD under the Associate Director for Diabetes, Endocrinology, and Metabolic Disorders. Under NIAMDD leadership, plans are made jointly for biomedical research programs, while recordkeeping identifies diabetes-related projects throughout the Institutes.

Planning can reflect a view of the totality of diabetes programs within the Institutes. In some cases, joint planning has led to cooperative project development: each year sees an increase in cross-Institute sponsorship of diabetes research. As many as nine separate Institutes have cooperated in announcing the availability of new awards for diabetes programs during 1979. These projects have been initiated in such diverse areas as epidemiology, psychosocial aspects, scientific training, obesity and nutrition, viral etiology, cardiovascular complications, and diabetic eye disease. These joint program announcements have placed special emphasis on diabetes. These projects, which the Institutes view as part of an ongoing NIH-wide effort to encourage diabetes research, are described in the sections that follow.

Cooperation has not been limited to the research area. Efforts are under way to bridge the gaps among research, education, and health care practices. In a number of instances these efforts are sponsored by multiple organizations. The Center for Disease Control has been working with state organizations, the Diabetes Research and Training Centers, and the Indian Health Service to provide training in diabetic care. The Department of Agriculture has worked with existing local educational programs concerning nutrition matters, including those related to diabetes. And a wide range of conferences and workshops have been conducted to acquaint participants from numerous organizations with the state of the art in diabetes research and health care. One example is the conference on behavioral and psychosocial issues in diabetes, and other examples of jointly sponsored conferences are described in the sections that follow.

Neither has cooperation been limited strictly to the governmental sphere. Many Federal agencies report developing active communication and joint endeavors with private voluntary organizations, especially the Juvenile Diabetes Foundation and the American Diabetes Association. Several examples of this cooperation are also described in the report.

Beyond cooperative planning, agencies are going further to actually commit financial, physical, and personnel resources in unison. The following descriptions illustrate some of the new cooperative Federal efforts to combat diabetes. In combination with ongoing efforts, it is hoped that these new undertakings will give added momentum to progress in diabetes research and service.

Cooperative Projects in 1979

Program Announcements in Diabetes Sponsored by Nine Institutes

Nine Institutes of NIH have cooperated once again to issue a joint program announcement in diabetes mellitus and related programs. The objective of this 1979 announcement was to stimulate an expanded national research effort as recommended by the National Commission on Diabetes. The announcement included the full range of diabetes-related topics, and several Institutes report that the response has been excellent, with a considerable increase in both the number of applications received and the scientific quality of the applications. The program areas emphasized in the announcements included aging; animal models; dental complications; diagnosis; environmental factors; epidemiology; etiology, natural history, and pathogenesis; genetic factors; glucose homeostasis; hormone synthesis and secretion; immunology, viruses; infants of diabetic mothers; mechanism of hormone action; metabolic regulation; neurologic complications; nutrition and obesity; ocular complications; pregnancy and diabetes; psychosocial aspects; renal complications; transplantation and artificial devices; treatment; and vascular complications.

Program Announcement in Epidemiology of Diabetes Made by Eight Institutes

Eight Institutes have issued an NIH-wide program announcement soliciting applications for epidemiologic research and training. The number of applications received has been encouraging, but it remains clear that epidemiologic study of diabetes could still be expanded. The new program announcement stresses the fact that there are many needs and opportunities for epidemiologic research in diabetes.

Among these opportunities are studies on the etiology of the various types of diabetes or of impaired glucose tolerance in population groups within which glucose tolerance may be associated with demographic, nutritional, environmental, prenatal, immunologic, infectious, or other etiologic factors. Such population groups might include discordant twins, siblings of diabetics, communities, migrant

groups, specific racial or ethnic groups, or case/control studies. Other possibilities include epidemiologic approaches to the natural history of the various types of diabetes; assessment of risk factors for each type; the causes of differences between groups in the frequency of development and extent of the complications of diabetes; epidemiologic assessment of the relationship between obesity and non-insulin-dependent diabetes; assessment of changes of glucose tolerance with aging; the relationship of gestational diabetes to subsequent overt diabetes; secular trend and geographic clustering of diabetes as an underlying and a contributing cause of death by age, race, and sex; evaluation of the socioeconomic costs of diabetes and its complications; and the problems of patient compliance in this chronic disease. Research that utilizes or builds on existing population-based or clinic-based data sets, where diabetes or glucose tolerance can be well defined, is particularly encouraged.

Improvements in Diabetes Data Capabilities

The National Diabetes Data Group and the National Center for Health Statistics (NCHS) are collaborating in extensive and detailed analysis of the data on diabetes and its complications already collected in NCHS surveys. They are also cooperating to redesign future surveys, so that a more accurate description of the epidemiology of diabetes and its public health impact in the United States can be obtained. Bureaus, Institutes, and Divisions with activities in the area of diabetes are being consulted regarding their views and needs with respect to this effort.

Five-Institute Program Announcement in Behavioral Studies Related to Diabetes

Four Institutes of NIH and the National Institute of Mental Health have issued a program announcement soliciting applications for research on the psychosocial and behavioral aspects of diabetes. The objective of the announcement is to encourage interdisciplinary studies between behavioral and biomedical investigators, and to define further the scope, depth, and influence of the disease and apply this knowledge to improved prevention, treatment, and control strategies. Among the areas in which study is encouraged are the following:

- The influence of stress on metabolic homeostasis and on diabetic complications;
- The influence of attitudes and beliefs on compliance with prescribed therapeutic regimens;
- Coping behaviors of the diabetic patient and/or the family of the diabetic;
- The psychosocial factors affecting diabetes therapy, including the impact of memory and other cognitive deficiencies often experienced by the elderly; problems associated with age-related decline in the sense of smell and taste and its effects on diet and appetite; and the influence of cultural beliefs and attitudes toward medical care;
- Predictor variables related to diabetes control and development of predictive tests to identify patients and families at risk for developing serious psychosocial problems or problems of compliance;
- Specific behavioral or psychosocial problems associated with special populations including the aged, children, adolescents, parents of diabetics, and American Indians;
- The effects of blindness or co-existent disease on the diabetic's ability to maintain appropriate medical and dietary management;
- Epidemiologic studies measuring the prevalence of psychosocial problems and family disruptions;
- Psychosocial effects of insulin-dependent diabetics on other family members, including studies of psychodynamics within the family; and
- The use and effectiveness of behavior modification and other psychosocial treatment techniques in dietary control.

Five Institutes and the National Diabetes Advisory Board Jointly Sponsor Psychosocial Conference

In spite of the well-recognized association between diabetes and behavior and psychosocial factors, the scope or depth of the problem area is not known, and there has been little research directed toward elucidating the interrelationships. To encourage the identification and study of behavioral and psychosocial factors associated with diabetes and its complications, a national conference was held.

The conference, "Behavioral and Psychosocial Issues in Diabetes," was held in Madison, Wisconsin, May 20-23, 1979. It was sponsored by the National Institute of Mental Health; the National Institute of Arthritis, Metabolism, and Digestive Diseases; the National Institute of Child Health and Human Development; the National Heart, Lung, and Blood Institute; the National Institute on Aging; and the National Diabetes Advisory Board. Leading diabetologists, behavioral scientists, and those who live with diabetes reviewed the emotional and psychosocial problems associated with diabetes and suggested specific approaches to address the problems.

Work group summary reports repeatedly suggested seven areas of recommendations:

- The need for rigorous research to integrate biomedical, clinical, and psychosocial interventions;
- The need for a therapeutic alliance team that includes the patient as an active participant;
- The need to educate practicing health care professionals about the emotional, psychological, and social issues associated with diabetes;
- The need for organizing and publicizing a variety of patient and family support systems;
- The need for a series of followup meetings to explore well-defined, diabetes-related behavioral topics;
- The need for adequate funding for professional training, research projects and conferences, and patient education programs; and
- The need for organized efforts to assure widespread professional and public understanding of the health and psychosocial aspects of diabetes.

Proceedings of the conference will be published in 1980. The volume will include the conference presentations, overviews of key issues and conceptual concerns for many of the psychosocial problem areas relevant to diabetes, workshop summary reports and recommendations, selected bibliographies, and descriptions of relevant NIH and NIMH research program announcements, manpower and training programs, and grant mechanisms.

Five Institutes Cooperate in Program Announcement of Overnutrition and Obesity

A program announcement entitled "Overnutrition and Obesity" was prepared by the staff of the National Institute of Child Health and Human Development in collaboration with those of five other Institutes and was published in November 1978. Several new projects were funded as a result of this programmatic initiative.

Four Institutes Emphasize New Programs in Research Training and Career Development in Diabetes

The National Institute of Arthritis, Metabolism, and Digestive Diseases and the National Heart, Lung, and Blood Institute have initiated a new manpower development award entitled Special Emphasis Research Career Award--Diabetes Mellitus: Cardiovascular, Endocrinologic and Metabolic Aspects. The award encourages researchers in the early stages of their careers to pursue research in these areas. The goal is to create a pool of highly qualified investigators for a future role in research, training, and clinical care.

The Special Emphasis Research Career Award on diabetic aspects of obstetrics, perinatology, and pediatrics was also published in November 1978. The awards will be sponsored jointly by the NIAMDD and the NICHD. The first group of applications is currently under review. A similar award is being developed by NIAMDD and NIA.

Cooperative Study of Virologic and Immunologic Aspects of Diabetes

As the virologic and immunogenetic mechanisms in the development of diabetes have gained prominence, the need for interdisciplinary approaches has grown. Coordination of activities among NIAID and other Institutes began with joint program announcements in a number of areas related to diabetes, including epidemiologic research. The NIAID's Epidemiology and Biometry Branch has subsequently convened a group of experts to identify research needs in epidemiology and virology, and plans have begun for an NIAID-NIAMDD cosponsored workshop on the immunobiology of diabetes. The workshop will allow scientists from different areas to discuss the ways in which immunologic progress can contribute to other areas of diabetes research.

In addition, intramural scientists at the National Institute of Dental Research (NIDR) are cooperating with investigators at Walter Reed Army Hospital, at the National Naval Medical Center, and at Mount Sinai School of Medicine in New York. They are studying the reaction of human pancreatic beta cells to potentially diabetogenic viruses, and to human autoantibodies from patients with acute-onset diabetes. Through their renal transplant units, the two military hospitals furnish human pancreatic tissue, so that NIDR scientists can isolate and culture human beta cells and study their susceptibility to virus infection and their interaction with human autoantibodies. The studies also examine the effects of modifying influences on these interactions. The NIDR intramural scientists are also cooperating with investigators at NIMH and NIAMDD in studies of subhuman primate pancreatic cells.

NIDR intramural scientists have also collaborated with scientists from NIAMDD in an *in vitro* study which showed that certain viral infections can reduce the number of insulin receptors on the surface of cells. A reduction in receptors *in vivo* would tend to aggravate the diabetes and its complications. The scientists have suggested that their findings offer one explanation for the poor regulation and increased insulin demand observed in diabetic children suffering from frequent colds and other infections. This work was recently published.

8 Building Relationships

CDC, NHLBI, and the Veterans Administration Cooperate in the National Eye Institute's Early Treatment Diabetic Retinopathy Study

Diabetic retinopathy is the complication most frequently responsible for loss of vision, causing 11.1 percent of all new cases of blindness each year. In part, retinopathy is characterized by generalized deterioration of the small blood vessels in the retina which may eventually lead to partial or total visual impairment. In the National Eye Institute's Diabetic Retinopathy Study which was completed about a year ago, it was demonstrated that photocoagulation treatment is effective in reducing the loss of vision in patients with moderate-to-severe retinopathy. This finding provided encouragement that even more vision loss might be prevented through treatment of early retinopathy. NEI has therefore recently initiated a new collaborative trial, the Early Treatment Diabetic Retinopathy Study, to study the efficacy of treatment in patients with less severe fundus abnormalities. Patients who meet the eligibility criteria for inclusion in the study and agree to participate will have one eye assigned randomly to early treatment. Treatment of the other eye will be deferred. Half of the patients will be assigned to drug therapy (aspirin in a low dose) and the other half to placebo. In addition to examining the effects of early interventions in reducing the ocular complications of diabetes, data on medical and cardiac events (non-fatal myocardial infarction) are also being collected and evaluated. The NHLBI has contributed funds for the purchase of electrocardiogram equipment and the Center for Disease Control, with funds from the NEI, is establishing laboratories in which specimens from the patients will be evaluated for drug compliance. The NEI is also providing funds to allow several VA Medical Centers to participate.

USDA Conducts Projects in Concert with State Experimental Stations, Local Departments of Health, and the Indian Health Service

Scientists in state experimental stations are studying the effects of the kind and amount of food intake on insulin function and various aspects of metabolism directly related to insulin function. Federal funds to land-grant universities have been used to conduct research in different animal models on genetics, dietary constituents, and hormones.

There have been limited cooperative efforts in nutrition education for the diabetic population with such agencies as state departments of health and the Indian Health Service in those states where there is a Native American population.

CDC Improving Communication with Diabetes Research and Training Centers and Many Federally Sponsored Local Programs

In 1979, the Center for Disease Control and the Diabetes Research and Training Centers (DRTC) in proximity to the program states increased the frequency and range of their interaction to include training of CDC project staff, consultation on medical and evaluation questions, and the dissemination of data and pertinent information of common usage.

Numerous, multilevel contacts have been maintained by CDC and their state projects with the National Institutes of Health; Area Health Education Centers; Health Services Administration; Health Care Financing Administration; Diabetes Information Clearinghouse; DMCC; American Diabetes Association; Juvenile Diabetes Foundation; American Association of Diabetes Educators; and local affiliates in both project and nonproject states. Both the CDC and DRTC programs are in developmental phases, and this early liaison is helping them cooperate to coordinate plans for joint projects of mutual benefit. All of the organizations involved look forward to continued cooperation and expect that this approach will allow each organization to accomplish program developments in concert which could not be accomplished by the individual organizations alone.

Cooperative Development of Indian Health Service Diabetes Control Programs

The Center for Disease Control, along with the National Institutes of Health and other Federal agencies, is assisting the Indian Health Service in developing a model diabetes control program. Several NIAMDD Diabetes Research and Training Centers are helping to train health care personnel for these programs.

CDC Cooperation Involved in Pregnancy Project

The Improved Pregnancy Outcome Project in Mississippi has involved coordination among many of the diverse institutions, official agencies, and voluntary organizations. Screening data from 2,000 persons are being analyzed and the results used to improve referral and followup.

Studies of Diabetes in Pima Indians Jointly Supported

Since 1965, biomedical investigators have been studying the Pimas, an Indian tribe researchers often refer to as a "genetically homogeneous population." The Pimas have the highest rate of diabetes ever recorded in a discrete population, and they are now the focus of a special multidisciplinary project. The National Institute of Arthritis, Metabolism, and Digestive Diseases and the General Clinical Research Center (GCRC) program, supported by the Division of Research Resources, are currently funding a research unit in Phoenix for the study of human diabetes. Although the primary work on the Pima project is being conducted at the NIAMDD-funded Phoenix Clinical Research Center, other support comes from an NIAMDD-supported

project at the University of Texas which includes collaboration among scientists at no less than 16 different institutions. Among these are the University of Geneva, Switzerland; the University of Chicago; the University of California at San Diego; Harvard University; the Salk Institute in California; and the Bronx, New York, Veterans Administration Hospital.

In addition, researchers at the University of Vermont's General Clinical Research Center have added their collaboration and support to the Pima project. Of particular interest to these investigators is genetic predisposition to obesity and its relationship to the diabetic state. The Pimas have both a high rate of diabetes and a high rate of obesity. Virtually all diabetic Pimas develop the non-insulin-dependent form of diabetes. About 90 percent of U.S. diabetics suffer from this type of diabetes, so results from the Pima studies should have implications for other diabetics.

Scientists at the National Eye Institute are providing ophthalmic consultation in collaboration with NIAMDD. This effort has recently resulted in demonstration of a positive relationship between diabetic retinopathy and elevated blood pressure.

International Study Encouraged

The NIAMDD and the Fogarty International Center have established a Senior Investigator Award in Diabetes which will enable midlevel and senior U.S. researchers to study diabetes-related problems in foreign laboratories and hospitals. Four awards have been made thus far.

III. Aims
and Accomplishments

In the past year there have been accomplishments in the full range of activity areas reported to the DMCC. From the most fundamental research to applied programs to improve the skills of health care providers, Federal programs have stimulated new discoveries and applied them to improve diabetes treatment and prevention. The variety and complexity of these accomplishments present a strong record of progress.

This chapter presents examples of noteworthy accomplishments. The examples were suggested by DMCC representatives to illustrate the progress that different organizations have recently made. It is hoped that the material included will give the reader an idea of the diversity of Federal efforts and the overall direction that Federal programs in diabetes have taken during FY 1979.

To help in understanding the nature of each organization's responsibilities, we have included a statement of each organization's mission as it relates to diabetes. This is followed by descriptions of achievements related to that mission.

National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD)

Mission

The National Institute of Arthritis, Metabolism, and Digestive Disease (NIAMDD) is the lead agency for federally supported diabetes research and is responsible for the planning, development, and implementation of a comprehensive national diabetes program. The Institute conducts and supports projects ranging from basic research to clinical investigations and large-scale clinical trials. Such studies include fundamental cellular and molecular studies, applied research, and investigations of the etiology, pathophysiology, epidemiology, and psychosocial aspects of diabetes mellitus. These efforts aim at gaining new knowledge and improving medical capabilities to diagnose, treat, cure, or prevent diabetes and its complications.

Support for basic and clinical biomedical research, as well as epidemiologic and behavioral studies, is provided through investigator-initiated research grants, program project and center grants, career development and training awards, and research and development contracts. Through the Diabetes Program Branch, the Institute also supports special programs and activities, such as the National Diabetes Data Group, the National Diabetes Information Clearinghouse, and various special research initiatives. In addition, the Diabetes Research Program provides grant support for a wide range of studies, including: structure and function of pancreatic hormones and related peptides and enzymes, their biosynthesis, secretion, and mechanisms of action; carbohydrate, lipid, and protein metabolism; and nutritional interrelationships and obesity. Other studies include the genetic nature of diabetes and attempts to identify markers which characterize individuals predisposed to diabetes. Additional areas of research include immunologic and infectious factors and studies of nutrition, metabolic regulation, and hormonal factors.

The Diabetes Centers Program administers two types of center awards, the Diabetes-Endocrinology Research Centers program (DERC) and the Diabetes Research and Training Centers program (DRTC). The DERC is exclusively oriented toward biomedical research, while the DRTC's include training and information transfer components as well. Both types of centers foster interdisciplinary cooperation among groups of established investigators. The primary requirement for establishment of either a DERC or a DRTC is a strong base of high-quality, ongoing biomedical research. In addition, DRTC's also have a training/information transfer component which includes training of both medical and allied health professionals, continuing education, model demonstration, and outreach activities. For both types of centers, the grant provides for core facilities (shared resources), pilot and feasibility studies (new initiatives), and limited funds for program enrichment. This funding is intended to strengthen existing programs, increase productivity, and foster the generation of new ideas and innovative research approaches.

The National Diabetes Data Group collects, analyzes, and disseminates data on diabetes and its complications. Among its concerns are defining data needs, coordinating data collection from multiple sources, making reliable data available to users, measuring medical and socioeconomic impact, and standardizing collection procedures and terminology.

The Data Group fosters, coordinates, and integrates national resources for collecting and analyzing data on diabetes. This group provides a central source of accurate, reliable statistics. These activities allow rational development of scientific priorities and public health program plans. The National Diabetes Data Group consists of a nationwide group of expert advisors including epidemiologists, individuals with expertise in the research, nutritional, and socioeconomic aspects of diabetes, and representatives from Federal agencies and voluntary organizations.

The National Diabetes Information Clearinghouse collects and disseminates information about educational materials, programs, and resources. It serves other government programs, voluntary organizations, and professional groups and it functions to improve access to information for these groups, patients, and the general public.

12 Aims

The National Diabetes Information Clearinghouse, in its initial period of development, has three major goals: to increase the availability of accurate diabetes information for health care professionals, for patients, and for their families; to increase community awareness and understanding of diabetes as a major health problem; and to establish a viable system for speedy communications about new developments, techniques, and programs in diabetes among all sections of the diabetes community. In cooperation with the Clearinghouse, the American Diabetes Association, the Juvenile Diabetes Foundation, and the American Association of Diabetes Educators are establishing criteria and a mechanism for evaluating nonscientific printed diabetes education materials. These groups are also cooperating with the Clearinghouse to define further the educational and informational needs of the diabetes community.

Diabetes research cuts across Institute and program boundaries and requires the cooperation of many groups to implement a comprehensive diabetes research plan. As a part of its coordinating efforts, NIAMDD's Associate Director for Diabetes, Endocrinology, and Metabolic Diseases serves as the chairman of the Intra-NIH Diabetes Mellitus Coordinating Committee, a subcommittee of the DMCC. The Intra-NIH Committee is crucial in fulfilling the NIH's role in planning and implementing the comprehensive programs of diabetes research.

Achievements

Progress in Developing Techniques for Transplantation of Pancreatic Islet Cells

In the transplantation of insulin-producing pancreatic islet cells, one of the major problems encountered during the last several years has been allograft rejection. Recently, however, grantees of the program have developed new techniques which markedly prolong the survival of rat islet allografts across a major histocompatibility barrier. This demonstration suggests that immune rejection may not prevent the development of islet transplantation as a successful therapy in animal diabetes, although a number of other significant problems remain before the potential clinical application of these procedures can be established for humans. Specifically, it will be necessary to (1) define further the mechanism of immune rejection and prevent its occurrence; (2) develop improved techniques for selective, mass isolation of beta cells from pancreatic tissue; (3) develop improved procedures for long-term storage of islet cells prior to transplantation; (4) evaluate further the relative advantages of various transplantation sites with regard to the specific survival and functional integrity of beta cells; and (5) assess the impact of successful transplants on plasma glucose control and other indices of metabolic homeostasis in diabetes.

Improvement in Insulin Delivery System

Another promising area of research interest is related to the development of improved devices for regulating the delivery of insulin to the diabetic. In this regard, two general types of mechanical devices are being developed. One of these, referred to as a "closed-loop" system, consists of a glucose sensor, an insulin pump, and a control circuit that regulates the rate of insulin administration as an on-line function of measured glucose. At the present stage of development, closed-loop systems are large, complex devices which require a substantial commitment of highly trained manpower and other specialized medical resources. In addition, such devices virtually immobilize a patient in a bed or chair and can therefore be used only on an inpatient basis for treatment of acute emergencies or for short-term experimental studies. Further development of refined, miniature, closed-loop systems is limited by a number of factors, including the lack of a reliable and specific glucose sensor with physical and biological characteristics that would make it appropriate for long-term studies.

The other type of insulin delivery device, the "open-loop" system, consists of an insulin pump and a control circuit that regulates the rate of insulin infusion according to a preprogrammed pattern. A number of prototype open-loop systems have been developed which are portable and offer the potential for use in long-term ambulatory studies. The program is providing increased support for the further refinement and evaluation of such systems that appear to offer the potential for improving plasma glucose in insulin-dependent diabetic patients to a greater degree than that achieved by traditional therapy. Such devices are still in the clinical evaluation stage and fundamental questions remain, including: (1) the need to assess alternate routes of insulin delivery, e.g., subcutaneous, intraperitoneal, intraportal, and peripheral venous routes; (2) development of appropriate computer programs for regulating insulin delivery in a manner that maintains metabolic homeostasis; (3) the need to develop biocompatible systems to avoid problems such as inflammation, clotting, tissue reaction, infection, and fever; (4) the problem of ensuring insulin stability during storage at room or body temperatures for prolonged periods in reservoirs/pumps/catheters composed of various foreign materials; and (5) the need to refine available pumps to ensure safe, accurate, reliable operation during long-term use by the diabetic patient. It is anticipated, however, that with further development these systems will help advance our understanding of the pathophysiology of diabetes and offer potential for future clinical applications.

New Knowledge of How Insulin Secretion Is Regulated

As suggested above, the regulation of insulin secretion represents an area of continued active research interest. Although glucose appears to be the primary physiological

stimulus for insulin secretion, it has not been established whether a metabolite of glucose or metabolic cofactor, or possibly glucose itself, acts as the actual trigger for insulin secretion. Nevertheless, studies have demonstrated that moderate-to-high concentrations of glucose directly or indirectly stimulate a biphasic release of insulin, starting with a rapid initial peak followed by a slower secondary rise. It has been suggested that these two stages of insulin release may reflect distinct phenomena, each under separate, possibly converging, regulatory control. Recently, rapid-phase insulin release, which appears to be defective in maturity-onset diabetes, has been observed for the first time in culture systems of isolated islets that retain normal beta- and alpha-cell function. Synthesis of D-glucose analogs is now in progress for use in studies with this culture system to further examine the structural characteristics of the glucoreceptors that regulate the secretion of insulin and glucagon.

There is also evidence that insulin secretion may be affected by a factor from the neuro-intermediate lobe of the pituitary gland which stimulates insulin secretion. This factor appears to be a corticotrophin-like peptide closely related to a fragment of ACTH. Results suggest that high insulin levels, partly under pituitary control, and high caloric intake may be interlinked and, in combination, could be a major factor in the early development of genetic obesity in experimental animals. It has also been shown recently that the chronic administration of porcine ACTH produces a syndrome similar to that displayed by the ob/ob mouse (hyperglycemic and insulin resistant). There is a single gene mutation in this mouse, and diabetes appears to be a relatively late consequence of the mutation. Insulin resistance does not develop until after hyperglycemia, while glucagon and cortisone are elevated well before hyperglycemia occurs.

Investigations of the mechanism of insulin action involve studies of both the binding of insulin to its target cells and the diverse effects of insulin on the cells. Considerable evidence suggests that insulin receptors located on the plasma membrane of target cells directly mediate the short-term effects of insulin on plasma membrane functions, such as glucose transport. Insulin also exerts a large number of diverse effects in the cells, and the timing of these events is important; some effects are immediate and some take hours to days. The discovery that insulin directly regulates its cell surface receptors has led to new insights into the mechanisms involved in several insulin-resistant and insulin-sensitive states. The mechanism for insulin's regulation of long-term effects on the cell interior is still unknown. One theory is that insulin, like glucagon, generates a second messenger at the cell surface which subsequently is responsible for the intracellular effects of insulin. Another theory is that insulin itself enters the target cell and that it, or a by-product, interacts directly with intracellular components. Recent studies support the theory that insulin does enter the cell and that intracellular organelles have specific binding sites for insulin. In this regard, one laboratory has reported evidence that isolated nuclei contain specific binding sites on the surface membrane.

The extent to which the mitogenic activity of insulin is due to interaction with its own receptor or with the receptors of nonsuppressible insulin-like activities, somatomedin, or multiplication stimulating activity has not yet been determined. Nevertheless, understanding the mechanism of action as well as interaction of insulin and insulin-like peptides is of considerable significance. One laboratory is constructing hybrid cell clones from cell lines that have only one or the other of these receptors and are defective in subsequent actions. Another grantee is looking at the effect of growth-promoting molecules on the process of cellular differentiation. It has been demonstrated recently that there is a significant polyploidization in the beta-cells of diabetic mice at 4 to 5 weeks of age when diabetic symptoms are emerging. It has been suggested that this phenomenon may be one of the earliest indicators of impending disease, reflecting some basic cellular defect.

Progress in Developing Animal Models of Genetic Aspects

Animal models are extremely important as tools for diabetes research. In this regard, it is not necessary that any given model duplicate every aspect of the human disease. It is likely that the primary metabolic disturbance in diabetes will be demonstrated in an animal where genetic modifiers can be more easily defined than in man. During the past year, the program has continued to actively solicit research grant applications proposing the characterization of such models. At the present time, studies are being supported to characterize at least 12 different animal models of diabetes, with primary emphasis on the ob/ob and db/db mice, the Chinese hamster, and the BB Wistar rat.

Improved Means To Produce Insulin for Research and Possible Clinical Applications

The synthesis of insulin using recombinant DNA techniques represents another area of active research interest. In this regard, one of the first practical spin-offs of recombinant DNA research has been the artificial creation of a form of rat insulin. More specifically, a team of scientists has used a copy of the rat's natural gene for induction of insulin synthesis in *E. coli* bacteria. This accomplishment was a forerunner of the subsequent production of a biological carbon copy of human insulin by another research team. If successfully developed, the new procedure holds potential for mass insulin production, alleviation of insulin allergy, reduced cost of treatment, and assurance of adequate supplies of the hormone for the diabetic population. Recombinant

DNA techniques also offer the opportunity to study the molecular basis for glucose regulation of insulin secretion. Studies in progress have recently demonstrated that the translation efficiency of pro-insulin messenger RNA is extremely sensitive to slight changes in the translation system. However, the actual relationship between this observation and deficiencies in insulin secretion *in vivo* has not been determined.

Progress in Defining Hereditary Differences Between Insulin-Dependent and Non-Insulin-Dependent Diabetes

With respect to the etiology of diabetes, genetic and epidemiologic studies have begun to provide some insight into the heterogeneous character of the disease. These studies clearly separate the genetics of the insulin-dependent from the non-insulin-dependent (adult-onset) form of diabetes. Studies with monozygotic twins reveal a striking difference in the concordance rates: for pairs of identical twins with non-insulin-dependent diabetes, it is only 50 percent. Some—although not all—studies on the population association between the HLA system (a system of inherited tissue-type markers found in white blood cells) and diabetes have shown that certain HLA alleles (genes that determine alternative characters in inheritance) appear with greater frequency in insulin-dependent diabetics than in the general population. The genetic factors associated with non-insulin-dependent diabetes appear, however, to be different, as evidenced by the fact that no such association between HLA type and this form of the disease has been observed. Studies in this area are continuing.

New Knowledge of the Relationship Between Viral and Genetic Factors in Diabetes Etiology

With respect to a viral etiology of insulin-dependent diabetes, it has been established that viral infections in experimental animals with certain genetic backgrounds may result in extensive pancreatic islet cell damage causing insulin-dependent diabetes. Several types of encephalomyocarditis virus have been shown to infect and destroy the pancreatic islets in certain strains of mice; other strains, however, are resistant to this viral infection. In addition, tissue culture techniques have demonstrated that the genetic constitution of the islet cell determines whether the virus can or cannot attach to the cell surface, penetrate the cell, and cause damage.

There is also evidence that viruses may play a role in some forms of insulin-dependent diabetes in man: a suggestive seasonal variation; development of diabetes in close association with some viral infections, such as mumps and rubella; and high titres of circulating antibodies to certain viruses. In addition, human viruses have been shown to be capable of inducing diabetes in animal models and damaging cultured animal beta cells; variants of two widely disseminated human viruses, Coxsackie$_4$ and Reovirus type 3, produced a diabetes-like syndrome in exposed and infected mice. Similarly, scientists at the National Institute of Dental Research have reported that two other human viruses, mumps and Coxsackie B_3, were able to infect and damage human pancreatic beta cells in culture. Recently, this group has also established that Coxsackie B_3 virus precipitated the onset of insulin-dependent diabetes in a 10-year-old boy. Although this work was not directly supported by the NIAMDD, it is noted here because of its potential significance to research in the field.

Evidence for an immunologic component in beta cell injury comes from the observation that most patients with insulin-dependent diabetes have circulating islet cell-specific antibodies (ICA), as well as from the above-mentioned association between HLA type and the disorder. This area of investigation is perhaps one of the best examples of the broad implications of sophisticated diabetes-related basic research. The initial promising results of studies on interrelationships of the genetic constitution, immunologic status, and susceptibility to viral infections in the insulin-dependent form of the disease are receiving increased research attention.

Diabetes-Related Studies Receive Increased Support

NIAMDD supports a large number of studies related to diabetes that do not apply to diabetes alone. These studies, especially in basic research, are central to understanding the fundamental processes of disease etiology as related to normal states of health. In the past year, the Institute has further increased its support of diabetes-related research in metabolic diseases, endocrinology, nutrition, arthritis, kidney, hematology, digestive diseases, and orthopedics. Altogether, the Institute supported 164 grants totaling approximately $12.1 million for extramural research projects which are expected to contribute to improving diagnosis, treatment, and prevention capabilities in diabetes.

Among the diabetes-related research projects are studies of the regulation of carbohydrate and lipid metabolism; synthesis, secretion, and mechanisms of action for endocrine pancreas hormones and hormones that interact with insulin; relationships between diabetes, obesity, and nutritional factors; the biochemistry and pathophysiology of connective tissues; diabetic nephropathy; and hemoglobin biochemistry and other hematologic correlates of diabetes and its complications. Research support for fundamental and clinical areas has also increased, especially in the metabolic diseases, endocrinology, and nutrition programs.

Diabetes Research and Training Centers Begin Communications Efforts

Since activities in the Diabetes Research and Training Centers (DRTC) training and information transfer component

are somewhat new, more formal communications have been initiated to foster program development. In the past year, centers have initiated a series of special meetings to become better acquainted with each other's training/information transfer programs and to focus attention on areas where cooperation may help. Such meetings have been held recently to exchange materials and methodologies. Each DRTC also participated in the recent National Conference on Behavioral and Psychosocial Issues in Diabetes and in a symposium sponsored by the University of Indiana DRTC on compliance research.

National Diabetes Advisory Board Recommends Information Transfer Activities for DRTC's

One problem faced by the DRTC's is the difficulty of obtaining long-term support for research projects dealing with training/information transfer activities. The National Diabetes Advisory Board formally recognized this difficulty and recommended that DRTC support should be expanded to include research studies in these areas. In response to this recommendation, a careful study has been made; as a result, the DRTC guidelines have been revised to allow limited support of training/information transfer research projects for a maximum period of 5 years to any one center.

Increase in Epidemiology Grant Applications

Recent programming efforts coordinated by the Director of the Diabetes Data Group have resulted in an increased number of grant applications proposing epidemiologic studies. Although the approval rate for these applications has been relatively low, six meritorious projects studying discrete populations in Australia, Israel, Massachusetts, Oklahoma, and Pennsylvania have been initiated. In addition, plans are now being developed for a workshop on chlorpropamide-alcohol flushing and diabetes, as this phenomena may serve as a genetic marker for non-insulin-dependent diabetics, which will facilitate epidemiologic investigations.

Development of Standardized Diagnostic and Classification Schemes

A major problem in assessment of the scope and impact of diabetes is the lack of a satisfactory diagnostic and classification scheme for the various forms of the disease. To address this issue, the National Diabetes Data Group has sponsored an international work group that formulated a consensus on a uniform classification of diabetes, appropriate diagnostic criteria, and a standard terminology to be used as a guide for clinical and epidemiologic research. During the past year, these proposals were widely circulated within the United States, and similar versions were reviewed abroad in an effort to obtain an international consensus. Recently, these proposals were endorsed by the Board of Directors of the American Diabetes Association and accepted by the Expert Committee on Diabetes of the World Health Organization.

Stimulation of Epidemiologic Study and Application of Epidemiologic Technique

In an effort to further stimulate interest in the epidemiology of diabetes, the National Diabetes Data Group and the National Institute of Child Health and Human Development cosponsored a symposium, "Childhood Diabetes and Diabetes in Pregnancy," at the annual convention of the American Public Health Association. Further, the Data Group has supported an analysis of the epidemiologic literature on obesity as a cause of diabetes, in order to assess research needs in this aspect of the etiology of adult-onset diabetes. In collaboration with the Statistical Bureau of the Metropolitan Life Insurance Company, the Data Group recently has estimated that the economic costs to the nation due to diabetes in 1977 approximated $6.8 billion. This estimate includes the direct and indirect costs of medical care of diabetics and earnings loss due to disability and death, but excludes costs associated with complications of the disease.

During the past year, the Data Group also has been working closely with officials from the Health Interview Survey, National Center for Health Statistics (NCHS), to analyze the surveys that have been collected to date and to prepare this data for publication in the medical literature. The information from these data sets should provide a more complete and accurate analysis of the epidemiology of diabetes than has been available in the past. The Data Group has also arranged for early analysis of the data on diabetes now being collected through the Health and Nutrition Examination Survey, NCHS. In addition, from data reported in the 1976 Health Interview Survey, the Data Group analyzed aspects of vision impairment for the Center for Disease Control in order to help establish priorities for diabetes screening programs. Further details on the NCHS data are discussed in the NCHS section of this chapter.

National Diabetes Information Clearinghouse Develops Specialized Bibliographies

During the past year, the Clearinghouse has compiled 11 annotated bibliographies in response to requests for information from health care providers, diabetics, and the public. These bibliographies, which range from 30 to 130 items, include topics such as care of the diabetic foot, educational materials for and about young people with diabetes, cookbooks for diabetics, and Spanish-language materials for diabetics. At the request of the National Diabetes Advisory Board, the Clearinghouse also has provided the Emergency Medical Services of the Department of Transportation with diabetic emergency materials appropriate to first responders. In addition, the Clearinghouse has developed a thesaurus of diabetes terms for libraries and other reference sources to

facilitate access to information related to diabetes materials. In response to a joint request from the American Diabetes Association and the Juvenile Diabetes Foundation, the Clearinghouse staff is compiling a handbook of diabetes terms modeled after the highly useful "Handbook of Heart Terms." In addition, at the request of the Indian Health Service, the Clearinghouse is coordinating development and production of a simple diet manual of ethnic Indian foods in an easily understood format.

New Training and Career Development Programs Begun

An adequate supply of well-trained scientists is necessary for continued progress in diabetes research. To assure that such a supply is available, NIAMDD carries out a number of manpower development activities. In the past year, these programs have continued their support for a full range of research training and career development areas, as well as initiating several promising new endeavors.

One special area of interest is training for physician investigators who are so crucial to clinical research. Unfortunately, the last few years have seen a significant decline in the availability of physician investigators. The decline in availability has been documented in several recent studies, and NIAMDD has responded to this problem by emphasizing awards to physicians who are preparing for careers in academic medicine and research.

Over the past few years, special efforts have been devoted to expanding training programs in diabetes and related areas. As a result, several dozen new institutional programs have been initiated since 1977, and over 50 persons are currently being supported by individual fellowships for research training at the postdoctoral level. Career development awards provide support for individuals who have completed their formal training but have not yet reached the status of independent, established investigators. To supplement ongoing programs, the Special Emphasis Research Career Award was developed as a joint endeavor of NIAMDD, NHLBI, NICHD, and NIA. Further details concerning this award are given in Chapter II of this report.

Division of Research Resources (DRR)

Mission

The Division of Research Resources (DRR) identifies and strives to meet the research resource needs and opportunities of the National Institutes of Health. The Division conceives, develops, and assures the availability of resources that are essential to the conduct of human health research. DRR administers and manages five programs that serve health researchers at universities, hospitals, and research institutes throughout the United States. These programs are General Clinical Research Centers, Biotechnology Resources, Laboratory Animal Resources, Biomedical Research Support, and Minority Biomedical Support. During FY 1979, three of these programs have supported diabetes research: the General Clinical Research Centers Program, the Biomedical Research Support Program, and the Animal Resources Program.

The General Clinical Research Centers Program is composed of 75 specialized centers in major hospitals throughout the United States where more than 3,000 protocols are pursued annually by clinical researchers. The program supports 80 percent of the research concerning inpatient care for the NIH. In addition, an extensive outpatient activity is conducted within the existing centers. The range of studies related to diabetes, on both inpatients and outpatients, varies from metabolism to organ transplantation. Approximately 85 percent of the Division's diabetes research is supported by this program.

The Division's Biomedical Research Support Program supports many pilot research projects, including exploration of new ideas by young investigators. It also provides central shared equipment, and improves and develops institutional research services and resources. Some of this support is for research in diabetes.

The seven major Regional Primate Research Centers, strategically located throughout the United States, provide a specialized environment for the study of human diseases using nonhuman primates (apes and monkeys). With the establishment of the largest nonhuman primate research center network in the world, the program's main mission is to identify primate models in which diseases can be studied and duplicated, their causes and effects documented, and effective means of prevention and treatment developed. One of the diseases studied under this program is diabetes mellitus.

Achievements

Progress in Developing Wearable Insulin Delivery Systems

Considerable progress has been made during the past year in testing and evaluating automated, wearable insulin delivery systems. A number of General Clinical Research Centers (GCRC's) in various parts of the country have been participating in prototype production tests of these devices with juvenile diabetics.

Other areas of reported progress that have been aided by GCRC efforts include advances in pancreas and islet-cell transplantation and the development and subsequent clinical trials of improved diet-exercise regimens for overweight non-insulin-dependent diabetics. Such studies, conducted

by a variety of sponsoring organizations, are heavily dependent on the research resources of the GCRC's.

Development of a Transplantable Human Insulin-Producing Tumor Cell Line

At one institution, Biomedical Research Support Grant funds have been used to develop a transplantable human insulin-producing tumor cell line. Potential applications for this tumor include its use for studies related to pathogenesis of diabetes and for development of biological systems for the large-scale production of human insulin.

Primate Models of Certain Diabetes Characteristics

The Division of Research Resources provides models, specimens, and tissue cultures, without which research conducted in other organizations could not be done. Some recently developed resources are of special importance.

The diabetes mellitus syndrome in *Macaca nigra* (Celebes apes) has been characterized, and analogies have been made with human diabetes. Normal clinical values and abnormal limits have been established to categorize the extent and severity of diabetes. Pathological complications, including atherosclerosis, cataracts, muscle microangiopathies, and infiltration of the islets of Langerhans have been noted.

Laboratory detection methods for diabetes mellitus in the California Primate Research Center's nonhuman primate colonies have also been continued, though no animals with diabetes mellitus have been detected.

Administration of somatostatin (somatotrophin release inhibiting factor) in baboons (*Papio cynocephalus*) has been observed to prevent the secretion of growth hormone customarily evoked by a variety of provocative stimuli, e.g., systemic administration of insulin, of L-dopa, and of arginine. Somatostatin administration was also found to inhibit the secretion of insulin and glucagon.

National Eye Institute (NEI)

Mission

The National Eye Institute (NEI) supports and conducts basic and clinical research on the causes, diagnosis, and treatment of blinding and disabling eye disorders. New knowledge about the normal and abnormal structures and functions of the eye and visual system is essential to understanding the causes of blindness and other visual disabilities. In the United States, diabetes is the major cause of vascular and circulatory abnormalities of the eye. The ocular complications of diabetes that eventually lead to blindness or visual impairment include retinopathy, cataract, neovascular glaucoma, and disorders of the vitreous.

The NEI supports fundamental research designed to elucidate the pathologic events associated with diabetic eye diseases, along with clinical trials to evaluate the effectiveness of various forms of treatment and epidemiologic studies to identify risk factors associated with ocular complications.

Achievements

Increased Emphasis on Ocular Complications of Diabetes

Diabetic retinopathy and similar retinal vascular disorders are characterized by changes in the basement membrane of retinal capillaries, excessive leakage of fluid from retinal vessels, and proliferation of newly formed blood vessels along the inner surface of the retina. The following are examples of the kinds of diabetic research programs supported during FY 1979.

- Basic and clinical research projects on physiological factors influencing blood flow, onset of edema, and capillary closure; angiogenic substances, their antagonists and inhibitors received increased support. Approximately 100 grants were funded at a cost of $10 million.
- Three epidemiologic studies were initiated to determine risk and protective factors for ocular and other microangiopathic complications in diabetics.
- Two Research Career Development Awards were granted to investigators involved in fundamental and clinical studies of diabetes.
- An NEI program announcement on research in diabetic retinopathy and related vascular disorders of the eye was released in the *NIH Guide* on February 15, 1979. This program announcement had two objectives (1) to provide examples of fundamental research areas requiring additional attention and (2) to reaffirm the interest of the NEI in fostering the training of laboratory scientists and clinical investigators. In addition, the NEI joined with seven other components of the NIH in issuing an *NIH Guide* announcement on the epidemiology of diabetes.

Progress in Developing Techniques for Early Detection of Vascular Changes Related to Diabetic Retinopathy

Recent progress has been made in the use of vitreous fluorophotometry for early detection of abnormal vascular changes in diabetic retinopathy. Vitreous fluorophotometry provides a quantitative evaluation of the disruption of the blood-ocular barrier(s) and is sensitive enough to detect changes in its stability even where other clinical signs might appear normal. If the results from the ongoing Early Treatment Diabetic Retinopathy Study show that photocoagulation treatment early in the course of diabetic retinopathy is efficacious, vitreous fluorophotometry may prove extremely valuable as a means of selecting patients for treatment.

New Techniques for Measuring Blood Flow in Advanced Diabetic Retinopathy

In advanced diabetic retinopathy, widespread vascular blockage is associated with markedly decreased retinal blood flow. Three techniques are being investigated as noninvasive methods for monitoring retinal blood flow. These are measurement of mean circulation time, measurement of pulsatile blood flow in the macula, and laser doppler velocimetry. Using the first two techniques, investigators have been able to demonstrate decreased blood flow and loss of pulsatility in diabetic patients with advanced retinopathy. This research approach can yield important information on the sequence of hemodynamic changes during development of diabetic retinopathy. The same techniques might be used to determine the effectiveness of localized treatments, such as photocoagulation, or systemic therapies, such as insulin or aspirin.

Improved Abilities To Study Changes in Retinal Capillary Cells

Biochemical studies of normal and abnormal retinal capillary cells have been facilitated by the development of techniques for isolating and culturing these cells. Both endothelial cells and pericytes from the retinal capillary can now be maintained in culture. Using this material, investigators have found that the two cell types can be distinguished histologically, immunologically, and biochemically. These findings should lead the way to studies that elucidate (1) the mechanisms responsible for thickening of the basement membrane, (2) metabolic pathways for the production of complex alcohols (polyols), and (3) other functional and biochemical properties of retinal vascular endothelial cells and pericytes.

Evaluation of Photocoagulation for Treating Diabetic Retinopathy

The NEI has also increased its support of clinical trials to evaluate experimental treatments for diabetic retinopathy and other retinal-vascular disorders. The results obtained from the Diabetic Retinopathy Study have established a scientific basis for the use of photocoagulation in the treatment of proliferative diabetic retinopathy. Further analysis of the data from this study continues to yield information on the natural history of the disease and its course in treated eyes. A recently published report summarizes risk factors for developing severe visual loss in absence of treatment; this analysis of risk factors can now be used by practitioners in selecting the diabetic patients who would be most likely to benefit from photocoagulation.

Planning for a new multicenter clinical trial, the Early Treatment Diabetic Retinopathy Study (ETDRS), was completed in 1979 and patients are being enrolled. The ETDRS is an outgrowth of the Diabetic Retinopathy Study which showed that photocoagulation can substantially reduce the risk of blindness in eyes with moderately advanced stages of retinopathy. The major objective of this study is to determine the best time during the course of the disease to administer photocoagulation or other therapies. In FY 1979, NEI supported the planning for this study and the establishment of the 20 participating clinics, a coordinating center, and a fundus photograph reading center.

The multicenter Diabetic Retinopathy Vitrectomy Study is also in progress. Vitrectomy is an operation for diabetic retinopathy in which cloudy, blood-filled vitreous and scar tissue are removed from the eye and replaced by a clear liquid. This surgical procedure is performed on patients who have already become blind as a result of severe vitreous hemorrhage from diabetic retinopathy. To date, 50 percent of patients who have had the vitrectomy procedure have had enough vision to read. Without the operation, only 10 percent of such patients have some useful vision.

In addition, the NEI also supports investigator-initiated clinical trials of therapies for related retinal-vascular disorders. These are the Branch Vein Occlusion Study; the Prematurity, Vitamin E, and Retrolental Fibroplasia Study; and the Macular Photocoagulation Study.

New Insights in Genetic Marker Studies

The various forms of diabetes are known to have a genetic basis. Researchers have been able to show that a presumptive gene for insulin-dependent diabetes is located near that part of the sixth chromosome where the human lymphocyte antigen (HLA) complex is located.

The data reinforce the belief that both genetic and environmental factors are involved in the development of diabetes. Many researchers are trying to identify and study the viruses and genes that together may make some children more susceptible to diabetes. In this case, the location of the gene for diabetes is particularly revealing because the HLA complex is involved in the immune response. Consequently, this finding supports linkage of environmental and genetic factors in the etiology of diabetes. There may be a variable response of the immune system to various environmental factors in people with different HLA genes.

Investigators supported by the National Eye Institute are further examining the observation that certain histocompatibility antigens and beta-cell alloantigens are present in a significantly higher proportion of diabetic patients than in the normal population. These studies are examining the relationship between the presence of histocompatibility antigens and the presence or absence of diabetic retinopathy. In addition, a long-term followup study is planned of a normal population that has histocompatibility antigens

commonly observed in diabetics but does not have diabetes. Studies of this type will be valuable in predicting susceptibility to diabetes and thus, by early intervention and education, the devastating effects of diabetic retinopathy can be reduced.

National Heart, Lung, and Blood Institute (NHLBI)

Mission

The National Heart, Lung, and Blood Institute (NHLBI) is mandated to provide leadership for a national program to attack diseases of the heart, blood vessels, lungs, and blood, as well as problems of blood resources. The Institute plans, conducts, fosters, and supports an integrated and coordinated program of research, investigations, clinical trials, and demonstrations. These efforts relate to the causes, prevention, diagnosis and detection, and treatment of and rehabilitation from these diseases. The Institute also supports research on the clinical use of blood and all aspects of the management of blood resources. In addition, the NHLBI supports training of manpower in the fundamental sciences and clinical disciplines for participation in basic and clinical research programs related to the Institute's mission.

While the National Heart, Lung, and Blood Institute does not have a direct programmatic focus on diabetes, it does support investigations that are diabetes-related. The metabolic effects and cardiovascular consequences of diabetes are studied as aspects of atherosclerosis, hypertension, coronary heart disease, peripheral vessel disease, arrhythmias, heart failure, shock, thrombosis, and lung disease. In addition, epidemiologic investigations and clinical intervention trials on coronary heart disease include studies of diabetes as one of the several predisposing risk factors.

Achievements

Continuing, Increased, and New Funding of Projects Related to Diabetes

In 1979, NHLBI continued to support 23 applications for research in cardiovascular disease as it relates to diabetes. The Institute also increased its support of research in heart disease, peripheral vascular disease, atherosclerosis, hypertension, and blood coagulation that is related to diabetes morbidity and mortality. Moreover, it has increased support for research studies already under way which are unique to diabetic macroangiopathy.

New activities have included initiating and funding, in conjunction with NIAMDD, the Special Emphasis Research Career Award in Diabetes Mellitus: Cardiovascular, Metabolic, and Endocrinologic Aspects, which is described in Chapter II.

Research Examples of NHLBI Diabetes-Related Programs

The Institute continues to develop and conduct several major clinical intervention trials of the treatment and prevention of morbidity and mortality from coronary heart disease. In trials about the effect of a beta-blocking drug and about coronary artery surgery in the treatment of coronary heart disease, diabetic patients are included in the studies. In the Multiple Risk Factor Intervention Trial, insulin-requiring diabetics are excluded, but those with glucose intolerance or those who are managed without insulin are included in the study. Information of interest to the treatment and prevention of coronary heart disease among adult diabetics may arise from these extensive and long-term trials, which collectively involve about 34,000 participants. These trials are described below.

Re-examination of the Framingham Heart Study Cohort

This study has followed the health of the population (ages 30 to 60 years at the time of entry into the study) of Framingham, Massachusetts, for 28 years. The aim of the study is to identify risk factors for cardiovascular disease. Approximately 5,200 original subjects (men, women, and their offspring) have been given in-depth medical exams every 2 years. The study has contributed much to our understanding of factors that predispose persons to heart attack and of the natural history of atherosclerosis and hypertension. For the 238 men and 246 women who either have had or developed diabetes in the 28 years of the study, risk of atherosclerosis is increased. Although diabetes increases risk of coronary heart disease in both men and women, the relative risk in women is much greater. The same relationship holds true concerning risk of diabetes for intermittent claudication.

Data Collection in Clinical Pathology and Morbid Anatomy ("the Honolulu Study")

This study was designed to assess coronary heart disease mortality and morbidity among 2,500 Japanese men in Hawaii to see whether their rates were intermediate between the low levels in Japan and the high levels on the U.S. mainland. The major aspects of this study are a series of examinations of the type used in the Framingham study and lipoprotein phenotyping; diabetes is one factor being studied. It has been shown, thus far, that the incidence of diabetes in the Honolulu group is higher than in a matched sample of men in Japan but not much different from a matched sample in San Francisco. Data are now being analyzed to determine the role of various changed socioeconomic factors and known risk factors contributing to coronary heart disease in this group of men.

20 Aims

Epidemiological Studies of Coronary Heart Disease ("the Puerto Rico Study")

This is a prospective epidemiological study that began in 1965 to investigate coronary heart disease mortality and morbidity in a cohort of 2,567 rural and 6,190 urban men aged 45 to 64. The major effort of this study is a series of Framingham-type examinations at 2- to 3-year intervals. Four examination cycles have been completed so far. A 12-year mortality followup now is being completed. Diabetes is one of the factors under investigation. The prevalence of diabetes is higher in the urban population.

Multiple Risk Factor Intervention Trial for the Prevention of Coronary Heart Disease (MRFIT)

This trial, initiated in 1972 for an anticipated duration of 10 years, aims to determine whether a significant reduction in mortality from coronary heart disease will result from a special intervention program designed to simultaneously lower serum cholesterol, reduce blood pressure, and eliminate cigarette smoking. The study group consisted of 12,000 subjects aged 35 to 57 who were selected for elevation of three risk factors—hypertension, hypercholesterolemia, and cigarette smoking—but who were free from previous coronary heart disease. Individuals with glucose intolerance are included in the study group. This trial utilizes a randomized, nonblind design with two groups and a fixed sample size. The experimental group is subjected to a modified fat diet, antihypertensive therapy, and education related to lifestyle and smoking. Individuals in the control group are referred to their own physicians for treatment.

Beta-Blocker Heart Attack Trial (BHAT)

Coronary heart disease and its complications account for over 600,000 deaths in the United States each year. Survivors of a documented myocardial infarction are recognized as having a high risk of dying as compared to the general population. Serious arrhythmias, occurring with or without evidence of a new infarction, are a common cause of death in this population. Theoretically, an agent that (1) can block the sympathetic nervous activity thought to be involved in precipitating sudden death and (2) has nonneurogenic antiarrhythmic properties might be expected to prevent or retard coronary heart disease complications such as arrhythmias and, in turn, decrease mortality due to coronary heart disease. This clinical trial aims to determine whether the regular administration of propranolol, a blocker of sympathetic nervous activity (i.e., a beta-blocker), to individuals who have had at least one documented myocardial infarction will result in a significant reduction of mortality from all causes during the followup period. This trial plans to utilize 4,200 men and women aged 30 to 69. For this randomized double-blind study, patients while in the hospital for an acute myocardial infarction will be recruited. Glucose intolerant individuals are included in the study. This program was initiated in 1977 for a 7-year duration.

Lipid Research Clinics: Prevalence Study

One of the programs concerning dyslipidemia (lipid diseases) operating as part of the lipid research clinics collects data on glucose intolerant individuals. This is an internationally-based study of the prevalence of dyslipidemias in defined populations. The study includes 10 clinics in the United States, 1 in Canada, 1 in Israel, and 2 in the Soviet Union. This is the first time that such a large-scale multicenter collaborative population study, using comparable methodology, has been undertaken. The large numbers and more defined methodology aim to enhance detection of dietary influences on lipid transport diseases where they exist.

Stanford Three-Community Study

This study has three major objectives: (1) to determine how groups of humans in their natural communities may be induced to change some of their living habits now thought to be associated with the occurrence of accelerated atherosclerosis; (2) to determine prevalence, cause, and significance of certain metabolic risk factors associated with coronary heart disease and stroke and their precursors; and (3) to relate the behavioral and epidemiological studies in order to identify high risk target subpopulations to identify the means of achieving behavioral modifications in this group and to plan a prospective intervention trial for primary prevention of coronary heart disease and stroke in such a group. Some members of the community are glucose intolerant. Both media campaigning and/or personalized intensive instruction treatment were used effectively to allow considerable optimism about the utility of these methods in affecting cardiovascular morbidity and mortality.

Collaborative Studies on Coronary Artery Surgery

This trial aims to compare coronary artery surgery with medical management in patients with coronary artery disease and to maintain a registry on all patients undergoing coronary arteriography whether operatively or medically managed. Males and females with ischemic heart disease who are under 67 years of age, some with glucose intolerance, are included in the study. A randomized, nonblind, sequential design is utilized in which 600 to 1,000 patients will be enrolled, treated, and followed for a period of 5 years unless primary endpoints (death or myocardial infarction) are reached before that time. The program was initiated in 1973; recruitment will continue through June 1981.

Antenatal Steroid Therapy in Prevention of Neonatal Respiratory Distress Syndrome

Respiratory distress syndrome is one of the leading causes of morbidity and death in the newborn. Premature infants

are at higher risk. In the United States, approximately 10 percent of all infants are premature and, each year, about 50,000 cases of respiratory distress syndrome occur. Diabetes in the mother increases the risk of birth of a respiratory distress syndrome infant. The object of the study is to determine the effect of corticosteroids administered 24 to 72 hours before parturition on the incidence of respiratory distress syndrome and to determine whether therapy has any adverse short- or long-term effects on the infant. This study began in 1976 and has a planned duration of 4 years.

Vascular Lesions of Diabetes in Oklahoma Indians

Vascular manifestations of diabetes are being studied in a large population of Oklahoma Indians as part of a multinational cooperative research program sponsored by the World Health Organization. The aim of the study, 1 of 14 being carried out throughout the world, is to determine the magnitude and character of the differences among populations in susceptibility to microvascular and macrovascular lesions. Using standardized methods data are being collected on 1,000 diabetics and a representative sample of nondiabetics, 35 to 54 years of age. Serum triglyceride levels are very high in Oklahoma Indians who are diabetic and these levels are closely related to blood glucose values. Preliminary data show considerable potential for the prevention of coronary disease and amputation in diabetics.

Quarter-Century Study of Glucose Intolerance

This study will determine the prevalence and 25-year incidence of cardiovascular disease manifestations by race in women diagnosed as being normal or having abnormal carbohydrate tolerance tests in association with pregnancy. The study is expected to characterize the source of the expected high rates for cardiovascular disease among diabetic women, as contrasted with the low rates, at least among white, nondiabetic women. The cohort of patients, 685 pregnant women identified in 1954 and 1960 at Boston City Hospital and Boston Lying-in Hospital as having "potential" diabetes, is a unique resource. Those, together with 328 controls, were tested annually for glucose tolerance until 1971. From 1977 to 1979, 1,000 patients were located and invited back. A mortality of 10 percent is reported in the case group compared with 5 percent in the control; hypertension is reported in 7.5 percent of the case group and 3.5 percent in the control; and coronary artery disease is found in 6.9 percent of the case group and in 2.8 percent of the control.

Glycemia, Other Traits, and Cardiovascular Death in 40,000 Persons

This is a prospective epidemiologic study on hypertension and atherosclerotic disease on a population of approximately 40,000 white and black men and women in Chicago, chiefly 25 to 64 years, to be followed for mortality outcomes for 10 years. Subsamples are being investigated in order to ascertain the effect independently, and in combination with other factors, of asymptomatic glucose intolerance, hyperuricemia, electrocardiogram findings, and tachycardia.

Microcirculation in Patients with Diabetes Mellitus

The changes in the distribution, number, and patterns in the microvessels of the conjunctiva for nondiabetic individuals and patients with diabetes mellitus are being studied. Methods have been developed for obtaining high resolution photographs of the conjunctiva, automatic scanning by a video raster-line scan, and the computer-based image analysis to quantify vascular spacing, branching lengths, vascular volume of larger venules, and texture. Data on 245 patients between ages 10 and 55 show significantly fewer microvessels below 30 micrometers in diabetics without regard to age or sex.

Blood Glucose, Hemoglobin A_{1c} and Diabetic Vascular Disease

This project is a prospective 5-year evaluation of glucose control in juvenile onset diabetic (JOD) patients to the development of microvascular disease and to classical risk factors that lead to macrovascular disease. It is reported that several measurements (at 2-month intervals) of glycosylated hemoglobin levels (hemoglobin A_{1a+b+c}) provide an accurate integrated index of blood glucose levels in diabetic patients over an extended period of time. Enrollment in the study consists of JOD patients and 64 control nondiabetic siblings. Quadriceps muscle biopsies have been obtained and basement membrane thickness analysis nearly completed. The changes in cholesterol as a component in circulating lipoproteins on two consecutive visits, when evaluated by multiple regression analysis, revealed that cholesterol and its components correlate significantly with age, and the cholesterol correlated significantly with changes in triglycerides. In contrast with adult mature onset chemical diabetes, there was no relationship of high density lipoprotein cholesterol to triglyceride levels.

In 23 percent of the study, patients with a rare genetic type of properdin Factor B were found. This genetic type exists in only 1.9 percent of the general population. It indicates that a genetic locus for insulin-dependent diabetes mellitus is very close on chromosome-6 to Bf and that Bf F1 is a marker for nearly one of four insulin-dependent diabetic patients.

Long-Term Study of Diabetic Vascular Disease

This project is investigating the incidence of peripheral atherosclerosis, extracranial arterial disease, and peripheral neuropathy in selected subgroups of patients with diabetes mellitus. A 5-year prospective study of diabetic vascular disease is being carried out using noninvasive testing techniques. These include segmental limb pressures, arterial

blood velocity patterns, exercise testing, oculoplethysmography, phonoangiography, and ultrasonic studies of the carotid bifurcation. Five hundred unselected diabetics are seen once or twice yearly to evaluate the factors that correlate with the development and progression of atherosclerosis.

National Institute of Allergy and Infectious Diseases (NIAID)

Mission

The National Institute of Allergy and Infectious Diseases (NIAID) conducts and supports research on allergic, immunologic, and infectious diseases, including research on the infectious and immunogenetic factors that may induce diabetes, and on the cause, diagnosis, and treatment of certain complications of diabetes.

The Institute conducts basic research in microbiology, immunogenetics, immunology, and allergy. Through its grants, NIAID supports basic research in these fields, particularly investigation of Coxsackie and other viruses that are candidate agents in the etiology of insulin-dependent diabetes, microorganisms, and the immune response in bacterial and fungal infections for which diabetics are at high risk, and histocompatibility antigens and other host immunogenetic factors.

The Institute also supports developmental research on transplantation, including pancreas and pancreatic islet-cell transplantation, developmental research on recombinant DNA and containment technology, and on histocompatibility antigen systems.

In addition, NIAID sponsors workshops on areas of interest, including virologic and immunobiologic processes underlying insulin-dependent diabetes, to encourage communication among scientists in different fields.

Achievements

Increased Understanding of Viral Involvement in Diabetes Etiology

The possible viral etiology of insulin-dependent diabetes received wide attention when Coxsackie B_4 virus isolated from a fatal human case produced pancreatic islet-cell damage and clinical diabetes in mice. One recent effort supported by NIAID has added to understanding the cell surface receptors for Coxsackie viruses and the involvement of these receptors in the inhibition of infection. This and other work on cell-virus interactions should be helpful in elucidating the role of viral infection of pancreatic beta cells.

Association of Histocompatibility Antigens and Insulin-Dependent Diabetes Investigated

There is a steadily growing body of evidence that certain histocompatibility antigens are associated with insulin-dependent diabetes. At least one investigator whose work has been sponsored in part by the Institute has contributed directly to the establishment of a relationship between diabetes and the HLA-DR locus of the major histocompatibility complex in man. A number of other scientists have continued to extend the tissue-typing resources necessary to refine the observations in diabetes. In addition, there have been advances in techniques for developing hybridomas—lines of fused cells producing highly specific antibodies. These resources provide solid foundations for further probing of the immunogenetic mechanisms of diabetes and other diseases.

Recombinant DNA Techniques Developed To Produce Purified Insulin in Quantity

Insulin of low allergenicity is not readily available at low cost to all who need it. Recently, attempts to produce large quantities of highly purified insulin have led to the promise of commercial production by using cellular machinery in microorganisms modified by recombinant DNA techniques. Through the Office of Recombinant DNA Activities, in cooperation with other supporting organizations, the Institute coordinates and oversees all facets of this research in the government. Part of this role has required NIAID evaluation and support of containment procedures in order to assure effective and safe large-scale production of insulin and other biogenic pharmaceuticals.

National Institute of Child Health and Human Development (NICHD)

Mission

The mission of the National Institute of Child Health and Human Development (NICHD) is to contribute to the health of all citizens through efforts to understand the biological and behavioral factors related to child health, maternal health, and human development. The primary emphasis of NICHD's effort is prevention of disease and disability.

The NICHD goal of disease prevention is accomplished in part through research aimed at ensuring maximum health during pregnancy, infancy, and childhood. It is in this preventive sphere that studies in diabetes become most relevant to the mission of the Institute.

Achievements

Rapid Growth of NICHD Diabetes Program

The diabetes program of NICHD has grown rapidly in the past few years. In FY 1975, the Institute supported only 13

research projects having a major focus on diabetes mellitus. Since that time, there has been a steady increase in both the number of projects and level of support for diabetes research grants and training programs. By FY 1979, the number of projects had increased to 84, with a 12-fold increase in funds. This growth in the diabetes program is the result of active programming and the initiation of four major research programs on pregnancy and diabetes.

Clinical Trial Assesses Efficacy of Controlling Serum Glucose To Prevent Diabetes-Related Complications of Pregnancy

Because stillbirths, neonatal deaths, and congenital defects threaten the outcome of pregnancies in diabetic women, the NICHD recently began supporting a carefully controlled prospective clinical trial of strict control of serum glucose throughout pregnancy, and of the effects of glucose control on the incidence of perinatal mortality, morbidity, and congenital defects.

It has been established that careful control of serum glucose during the latter half of diabetic pregnancies reduces the risk of perinatal mortality. It is not known, however, if tight control in the first half of pregnancy would improve the prospects of favorable outcome, in regard to both infant survival and congenital defects. A recent clinical trial is designed to answer those questions.

The experimental design of the clinical trial involves random assignment of diabetic women very early in pregnancy in two treatment groups. One group receives intensive treatment, and the other receives the standard management. Women in the intensive treatment group are hospitalized for 2 weeks as soon as pregnancy has been diagnosed, and their concentrations of serum glucose are measured frequently. Their level of serum glucose is maintained between 70 and 140 mg/dl. Patients in the standard management group are not hospitalized during their first trimester of pregnancy.

Neonatal evaluation consists of thorough physical and neurological examinations, including a search for congenital defects. The success of normalization of serum glucose throughout pregnancy will be related to the incidences of perinatal mortality, morbidity, and congenital defects. This important clinical trial will document the impact of intensive diabetic management throughout pregnancy on fetal outcome and infant survival. The study, therefore, carries great implications concerning the scope and specifics of clinical management of diabetic pregnancies.

Creation of "Major Research Programs"

The National Institute of Child Health and Human Development recently funded four Major Research Programs (MRP's) which focus on various aspects of diabetic pregnancies and infants of diabetic mothers. In FY 1979, nearly $2.8 million were expended on these four MRP's. The impetus behind the formation of the Major Research Programs is expressed in the Congressional language of Senate Report 94-366. This report directs the NICHD to create Major Research Programs for mothers and infants in order "to undertake concerted biomedical and behavioral research efforts directed toward infant survival. . . ."

In carrying out this Congressional directive, the NICHD mounted a major research thrust in the area of diabetic pregnancies, since the outcomes of these high-risk pregnancies contribute significantly to the overall rates of infant mortality and morbidity in this country. The average insulin-dependent diabetic woman has, at best, only a 90 percent chance of success in delivering an infant who will survive beyond the age of 1 month and the chance of her infant's having a congenital defect is about 13 percent, or more than twice the risk faced by a nondiabetic mother. In addition to responding to Congressional directives regarding infant mortality, the creation of these MRP's also responds to the recommendations made to the NICHD by the National Commission on Diabetes Mellitus; namely that the NICHD support long-range followup studies of infants of diabetic mothers.

Each MRP has one major research objective. Collectively, the MRP's address the following objectives:

- Study of the concentrations and disposition of metabolic fuels as they affect fetal development and pregnancy outcome;
- Study of abnormal fetal metabolism and its effects on development;
- Study of abnormal carbohydrate metabolism from a developmental perspective; and
- Comprehensive study of diabetes in pregnancy and in the infants of diabetic mothers.

Studies of the Genetic Determinants of Diabetes

The NICHD is currently funding a contract entitled "Genetic Linkage Analysis of Juvenile Diabetes Mellitus." The contractor has made impressive progress and has already gathered new information about genetic marker associations with insulin-dependent diabetes mellitus (IDDM) and about patterns of segregation of genetic markers within families of diabetics. In its short existence, the project has proved itself to be a valuable resource for investigators who are working to discover the etiology of IDDM. Researchers are able to use the contractor's extensive collection of sera taken from families of diabetics for analysis of preinfectious, acute, and convalescent titres of

antiviral antibodies. The valuable serological collection, which represents extensive diabetic pedigrees, can also be used to confirm or deny reports of other workers who are searching for associations of genetic markers with IDDM.

Investigation of Fetal Endocrinology and Diabetes

Diabetes mellitus in association with pregnancy is frequently complicated in the fetus by a syndrome which includes fetal mortality, macrosomia, visceromegaly, extramedullary hematopoiesis, and islet hyperplasia. A number of model systems of maternal diabetes have been investigated in an attempt to provide insight into the casues of this abnormal fetal development. These studies are intended to explore the effectiveness in a pregnant diabetic animal model of fetal pancreas transplantation in providing an *in utero* environment consistent with normal fetal development. Specific organ systems are being studied by immunoassay, ultrastructural analysis, immunocytochemistry, and quantitative morphometry. Morphological and biochemical changes in these organs are being examined in relation to the severity of maternal diabetes, and in relation to the degree of reversal of the diabetic state attained by transplantation.

It is hoped that the proposed studies will establish the utility of islet cell transplantation beneath the renal capsule in providing an animal model which avoids exposure of the developing fetus to diabetic agents and can be used to study the interaction between maternal carbohydrate intolerance and fetal development. These studies also seek to answer the question of whether or not transplantation, as a means of reversing diabetes, eliminates or modifies the complications of diabetes associated with fetal development, and may provide the basis for future clinical transplantation in human diabetic females.

Studies of Fetal Lung Development in the Diabetic Pregnancy

Another current NICHD study is examining the process of fetal lung maturation in the diabetic pregnancy. The investigator hopes to ascertain why infants of diabetic mothers show increased susceptibility to respiratory distress syndrome, whether the risk for development of this disease can be accurately determined prenatally, and whether it can be prevented. The objectives are to study the complete spectrum of phospholipids in amniotic fluid specimens obtained from various pregnancies, including uncomplicated gestations, diabetic pregnancies, and other high-risk pregnancies; and to examine fetal and neonatal lung samples from Rhesus pregnancies complicated by maternal glucose intolerance by physiologic and biochemical techniques. The basic hypothesis is that when maternal diabetes complicates fetal development, a metabolic abnormality occurs in fetal lung, leading to defective synthesis and/or fatty acid composition of surfactant phospholipids.

Animal Studies of Fetal Pancreatic Islet Development in Diabetes

A recent study is examining the original and functional differentiation of fetal mouse pancreatic islets, and the effect of maternal diabetes on fetal cell development. The objectives are to define the normal functional differentiation of mouse pancreatic islets, to define the embryonic origin of mouse pancreatic islets of Langerhans, and to study the effect of maternal diabetes on the functional distribution of fetal pancreatic islets. The major tool used is the peroxidase-labeled antibody method. The coupling of specific hormonal antibodies to horseradish peroxidase for use with the light and electron microscope provides a probe for investigating the development of these hormones. The time of onset of hormone synthesis as well as identification of the cells responsible for particular hormone synthesis are investigated in fetuses of normal and diabetic mothers. It is hoped that knowledge of the effect of maternal diabetes on the development of fetal pancreatic islets will increase our understanding of islet cell hyperplasia and the marked hyperinsulinemia in children born to diabetic mothers.

National Institute of Dental Research (NIDR)

Mission

The mission of the National Institute of Dental Research (NIDR) is to conduct, foster, and coordinate research into the cause, prevention, diagnosis, and treatment of oral and dental diseases and conditions. NIDR accomplishes this mission by awarding grant and contract funds to support a broad range of biomedical research which includes basic laboratory studies as well as applied clinical projects. The Institute's primary responsibility in relation to diabetes is to support research on the dental complications of diabetes. However, as part of the National Institutes of Health, NIDR also assumes the responsibility for developing basic biologic knowledge which may not seem obviously relevant to oral diseases. Thus, NIDR intramural studies include studies on human viruses as potential etiologic agents in certain types of diabetes, as well as studies on the biochemistry of normal basement membranes. The dental complications consist of increased susceptibility to periodontal diseases and to oral candidiasis, increased frequency of cleft palate in offspring of diabetic mothers, increased alveolar ridge bone loss in edentulous individuals, and the development of peripheral orofacial neuropathies, including losses in salivation, taste, smell, and mucosal sensory perception. The NIDR extramural programs support research on some, but not all, of these complications. Current research includes studies on altered collagen metabolism and impaired polymorphonuclear leukocyte function in humans and animals afflicted by diabetes and periodontal

disease, and studies on peripheral neuropathy in diabetic animals. NIDR's National Caries Program supports contract and grant studies to develop new artificial sweeteners. Although these studies were initiated to develop safe compounds to aid in the dietary control of tooth decay, such compounds could also be applied to the dietary control of diabetes mellitus.

Achievements

Virus Shown To Cause Juvenile-Onset Diabetes in Genetically Susceptible Individuals

The most significant finding made by NIDR scientists in FY 1979 was the recovery of a diabetogenic human-type virus from the pancreas of a 10-year-old boy with acute-onset diabetes. This virus, identified as a variant of Coxsackie virus B_4 was subsequently shown to be capable of inducing diabetes in susceptible strains of mice. These findings constitute the first direct evidence that a virus can cause juvenile-onset diabetes (JOD) in humans.

Several years of background preparation set the stage for this discovery. NIDR intramural scientists had developed animal models for virus-induced diabetes mellitus similar in many respects to JOD of humans. In further studies they showed that genetic factors, inherited as an autosomal recessive trait, controlled the susceptibility to diabetes of these inbred strains of mice; that beta cells from both animals and humans could be grown in culture so that the interactions of viruses with these cells could be studied; and that variants of a number of viruses (including Coxsackie virus B_4) from the human population could produce diabetes in susceptible strains of mice. These laboratory results, together with the case report cited above, indicate that human virus infections can initiate the onset of juvenile-onset diabetes in a certain group of genetically susceptible individuals. The magnitude of the population that could be affected by such an environmental agent is unknown, but it is believed to be small. Since the results described above suggest that other human viruses might also be implicated in diabetes, the NIDR has awarded a 2-year contract to screen a number of human viruses and their variants for the capacity to cause diabetes in the mouse model system. Diabetogenic viruses identified in this project will then be tested for their capacity to infect human pancreatic beta cells.

Investigation of the Role of Autoantibodies in Diabetes Etiology

Intramural scientists have developed techniques to determine whether autoantibodies found in the sera of patients with juvenile-onset diabetes play a role in the etiology and pathogenesis of this disease. They have found that islet-cell antibodies and the anti-insulin antibodies can be readily detected in Bouin-fixed paraffin-embedded human pancreas. These autoantibodies are now being studied in a well-defined microculture system for their capacity to damage murine islet cells *in vitro*.

Improved Knowledge of Tissues Related to Blindness and Diabetes

In diabetic retinopathy, it has been observed that there is a progressive thickening of the basement membrane. Intramural NIDR scientists are studying the components, structure, and biosynthesis of basement membranes in normal developing tissues as well as in diseased tissues, including tissues from diabetics. So far, they have isolated and characterized several specific proteins from basement membrane. These scientists are also carrying out studies on the migration of cells from normal and diabetic individuals, particularly in regard to wound healing.

New Knowledge of How Diabetes Affects Bone Development

In other intramural projects, investigators have found that the development and metabolism of bone are impaired in diabetes. Osteoporosis among the diabetic population appears to be common. Recent work has demonstrated impaired endochondral bone growth and development during streptozotocin-induced diabetes. In these studies, scientists observed that there was inhibition of mesenchymal cell proliferation, decreased and delayed cartilage formation, and decreased and delayed bone differentiation. In future studies they will focus on the early effects of insulin and insulin-like growth factors and polypeptides, such as somatomedin on mesenchymal cells, chondrocytes, and osteoblasts *in vivo* and *in vitro*. The scientists will pay special attention to intracellular loci of action by electron micrograph autoradiography of ^{125}I-insulin and related polypeptides in collaborative studies with the Intramural Diabetes Branch, NIAMDD.

Data Confirm Hypotheses That Diabetes Patients Have More Severe Periodontal Disease

Although the belief that diabetics have more severe periodontal disease than nondiabetics still rests primarily on anecdotal evidence, investigators have recently obtained preliminary data which tend to confirm this notion. In a current project, clinical investigators have studied 100 juvenile diabetic patients who presented themselves for general treatment at a hospital. The investigators found that approximately 15 percent of these individuals had severe periodontal disease. Those who had the most severe periodontal disease also had required the most frequent hospital admissions for diabetic complications, which sometimes included ketoacidosis. However, others had no apparent complications except periodontal disease. The initial impressions of the clinical scientists is that these patients are poorly controlled. The investigators now question whether

the diabetes is aggravating the periodontal disease, or vice versa. The type of periodontal disease observed in the juvenile diabetic was similar to that seen in the unique oral condition known as periodontosis, or localized juvenile periodontitis. In periodontosis, severe alveolar bone loss occurs bilaterally around first permanent molars and permanent incisor teeth in youth who also show an intrinsic impairment of neutrophil chemotaxis and phagocytosis but no other medical findings. The diabetic patients showed a similar pattern of molar/incisor bone loss, which in some cases was bilaterally symmetrical. The relationship between this localized pattern of bone loss and the white cell functional impairment in both diseases will be studied further.

These investigators have also identified 16 adult patients who have a strong family history of diabetes and who suffer from severe periodontal disease. Eight of these patients were found to have peripheral neutrophils with reduced chemotactic capacity. These findings indicate that further studies on the inter-relationships among diabetic family history, periodontal disease, and peripheral white cell abnormalities are warranted.

Association of Diabetes, Periodontal Disease, and Disturbances of Collagen Metabolism

Early in FY 1980, the NIDR expects to fund an approved grant project to investigate some of the questions raised by previous studies of diabetes and periodontal disease. In addition, NIDR will study the microbiology of periodontal disease and the competence of the immune system in diabetics.

The studies already cited indicate that diabetics have more severe periodontal disease because of alterations in the host response. However, other evidence indicates that their increased susceptibility may also be due to disturbances in collagen metabolism which would interfere with wound healing capacity. Using streptozotocin-induced diabetes in the rat as an experimental model system, investigators have shown that there is a net decrease in collagen synthesis in the skin, aorta, and gingiva of the diabetic rat, and a decrease in the degradation of collagen in the gingiva. In these experiments, the collagen mass in the gingiva of periodontally healthy diabetic rats remained constant, but the rate of turnover was greatly reduced. The scientists also found that streptozotocin-induced diabetes did not cause any specific effect on the type of collagen synthesized. There was no change in the Type I/Type III ratio, nor in the extent of hydroxylation. Thus, the investigators concluded that the primary effect of this form of experimental diabetes is to retard both synthesis and degradation. Thus, in any host response to injury, including periodontal disease, tissue repair would be slower than normal.

Peripheral Neuropathy Studies Suggest That Diabetes Affects Hormones Related to Hirsutism

In continuing microscopic studies of peripheral neuropathy in diabetic mice, investigators have obtained evidence that the hypogonadism of the disease alters the submandibular gland and its innervation, and results in feminization of the male and masculinization of the female. The observations in the salivary glands and in the kidneys suggest an increase in testosterone production in females. The authors claim that their findings represent the first experimental histochemical observations which could be related to the increased androgen levels and hirsutism found in human female diabetes mellitus.

In previous studies on the diabetic mice, the same investigators had reported sensory ataxia coupled with marked Schwann cell proliferation in the trigeminal ganglion. Recently, the same finding was made in the sciatic nerve. Signs of degenerating myelin were also observed in this study. These investigators have recently begun to study the effects of this form of hereditary diabetes on the teeth and periodontal tissues of the mice.

National Institute of Environmental Health Sciences (NIEHS)

Mission

The National Institute of Environmental Health Sciences (NIEHS) grant activity related to diabetes seeks to explore relationships between exposures to environmental agents and changes in pancreatic structure and function.

Achievements

One grant was active in FY 1979, a portion of which assessed the pancreotoxic effects of environmental exposures to lead in animals and humans.

National Institute of General Medical Sciences (NIGMS)

Mission

The National Institute of General Medical Sciences (NIGMS) supports research in the basic or general biomedical sciences that have significance for two or more Institutes. Research relevant to diabetes would therefore either be of a kind also relevant to other categorical interests and diseases, or serve to illustrate general biological principles. The Institute support in this area is exclusively extramural through grants (including center grants) and contracts and is distributed among the four program areas: Pharmacology-Toxicology, Genetics, Cellular and Molecular Basis of Disease, and Physiology and Biomedical Engineering.

The Pharmacology-Toxicology Program supports studies that include the effect of drugs on the release of pancreatic and pituitary hormones and on carbohydrate metabolism, the interaction of hypoglycemic drugs with other drugs, untoward side effects of hypoglycemic agents, synthesis of new hypoglycemic agents, and the effects of diabetes on the pharmacology of drugs in general.

The Genetics Program includes studies on the cellular differentiation of the pancreas. Support is also provided for a diabetes cell collection in the Human Genetic Mutant Cell Repository which NIGMS funds under a contract with the Institute of Medical Research in Camden, New Jersey.

The Physiology and Biomedical Engineering Program provides a modest amount of support for research on implantable glucose sensors, which may ultimately lead to the development of a practical "artificial pancreas" for diabetic patients. Also included is work on the epidemiology of diabetes, intermediary metabolism in trauma victims or during anesthesia, and the response of diabetic patients to anesthesia.

Achievements

Maintenance and Provision of Cell Lines for Diabetes Research

Although the basic genetic defect(s) for diabetes have not been elucidated, the use of HLA system properties, insulin receptor properties, etc., have led to the suggestion that the disease can be studied in cell culture. In fact, cultured fibroblasts and lymphoblasts have now been shown to express the various HLA antigens as well as the insulin receptor. Therefore, to stimulate research in diabetes using cultured cells, the NIGMS established a collection of lymphoblast and fibroblast cell lines from well-documented diabetic families and individuals as a part of its Human Genetic Mutant Cell Repository at the Institute for Medical Research in Camden, New Jersey.

The collection contains an extensive family with maturity-onset diabetes and six families with a history of classical juvenile-onset diabetes. In addition, cultures were established from one family with juvenile-onset diabetes with optic atrophy. The diabetes collection also contains cell lines from the Pima Indians of Arizona, a population with an unusually high incidence of maturity-onset diabetes.

The Human Genetic Mutant Cell Repository contains 147 cell lines in the diabetes collection available to qualified investigators. The study of cultured cells offers not only the possibility of characterizing the cellular expression of the diabetic phenotype but also, with application of new techniques, an understanding of the genotypic defects as well.

Development of Sensitive Measures of Glucose Concentrations

Grantees of the Physiology and Biomedical Engineering Program have developed an immobilized enzyme sensor which has the unique feature of detecting glucose accurately at concentrations ranging from 1,500 mg glucose/dl to zero in either whole blood or plasma. The instrument is undergoing clinical evaluation; four patients have had their glucose continuously monitored for up to 5 days. The anticipated uses in the clinical setting could include monitoring of acutely ill diabetics, diabetic mothers undergoing childbirth, or diabetics undergoing major surgery. In addition to use in clinical research protocols, the sensor is a challenging component to engineer into the artificial pancreas. No other analytical method in use today has such a wide range of activity or can claim such accuracy and precision.

National Institute of Neurological and Communicative Disorders and Stroke (NINCDS)

Mission

The National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) has responsibility for conducting, fostering, and coordinating research on the causes, prevention, diagnosis, and treatment of the neurological, sensory, and communicative disorders. Within the scope of this responsibility, NINCDS conducts and sponsors basic, clinical, and epidemiological research as well as research training, in a variety of neurobiological disciplines encompassing metabolic, toxic, endocrinological, biochemical, physiological, morphological, pathological, immunological, vascular, behavioral, and microbiological studies as they relate to the understanding of the natural history of diabetes and its complications in the central and peripheral nervous system (including the autonomic nervous system).

Achievements

NINCDS maintains and augments its extramural and intramural research momentum in diabetes-related studies in order to explore the neural consequences of diabetes mellitus, the neuronal regulation of islets and other organs of peripheral carbohydrate metabolism, and the central nervous system control mechanisms regulating nutrient homeostasis. In so doing, the Institute is reacting responsively to the recommendations of the National Conference on Diabetes held in 1979 and to recommendations of the National Commission on Diabetes, the National Diabetes Advisory Board, and the DMCC.

The NINCDS diabetes-related budget increased from $1.6 million in FY 1976 to an estimated $5.3 million in FY 1981.

Its research fellowships and special awards increased to more than 22 in the area of neurobiology and muscle disease, etc. Thus, it is not unreasonable to expect that such training resources in basic and clinical research would encourage pursuit of research in a variety of specialized fields, including diabetes-related studies.

The Institute has expanded its extramural research on the physiopathogenesis of the neurological complications of diabetes. Pursuing a multidisciplinary approach to studies of diabetic peripheral neuropathy in humans, and in diabetic animal models, the NINCDS continues to develop techniques for the quantitative assessment of peripheral and autonomic nerve function as endpoints in the evaluation of the effects of long-term blood glucose control in diabetes; develop and evaluate drugs and other compounds to test various metabolic hypotheses in the etiology of diabetic neuropathy (aldose reductase inhibitors, myoinositol, etc.); conduct research work at the cellular level (biophysical, biochemical, and pharmacological) to define the neuronal and humoral control mechanism of islet cell secretory output; develop studies of the pharmacology and physiology of brain and gut neuronal and humoral agents that participate in the bidirectional interactions between the pancreas and the central nervous system and between the pancreas and the gut; explore the development of therapeutically and investigationally useful antagonists that influence islet cell function; investigate the localization of peripheral afferent inputs involved in the control of glucose homeostasis; identify central nervous system pathways that process information relating to metabolic status; enhance research to characterize biologically active substances in the brain, and unravel their function in normal and diabetic subjects; develop methods to alter function of neuronal pathways involved in caloric and glucose homeostasis and metabolic control; assess the interaction between psychological and physiological variables that contribute to the diabetic state; study vascular permeability, endoneural pressure, axoplasmic flow, and myelin composition in experimental animals; utilize immunologic techniques to assign cellular responsibility for segmental demyelination and assess the role of viruses in inflammatory neuropathy; and conduct studies of lipid composition of nerve and the effect of modification of membrane lipids with special focus on diabetic neuropathy and other neuropathies, including a number of genetically determined diseases in man and animals as well as human and experimental heavy metal intoxication and inflammatory disease.

One ongoing study explores whether there is accumulation of alcohol sugars in damaged fiber in diabetes; another explores whether there is a decrease in myoinositol in peripheral neurons. Since diabetics may not be rigorously controlled in regard to blood sugar levels to avoid hypoglycemia, and increased blood sugar levels might interfere with neuronal metabolism, animal and human studies are being conducted to evaluate (tight) blood sugar levels versus usual diabetic therapeutic levels. Such studies are concerned with such topics as central nervous system plasticity, modalities of management of patients in coma, permeability of the blood-brain barrier, cerebral circulation, feasibility of sensory prostheses, the underlying hormone and enzymatic mechanism involved in connective tissue, and arthritis-related disorders.

NINCDS conducts intramural research on the effect of ischemic metabolic derangements on the function of central and peripheral nervous system tissues, including a study of the use of phthalazinol, a cAMP-phosphodiesterase inhibitor used in treating amyotrophic lateral sclerosis. An acute effect of the drug on the polypeptide-protein composition of cerebral spinal fluid points out the importance of determining whether the enhancement of that polypeptide-protein in response to phthalazinol is specific to amyotrophic lateral sclerosis, or to amyotrophic lateral sclerosis in the presence of insulin-requiring diabetes with which it is sometimes associated. Research is being done using immunocytochemical techniques to localize myelin proteins and to study their distribution during myelination and demyelination in order to understand idiopathic polyneuritis and other types of neuropathy including those that occur in diabetes.

In addition, the Institute is exploring the relationship between diabetes and stroke. Since the physiopathology of cerebral occlusion differs from that of coronary occlusion as to underlying mechanism and its relation to diabetes, the Institute is developing a protocol for a clinical trial to elucidate this relationship. Further, positron emission transverse tomography, a new technique using radioisotopes and a scanning methodology, is being utilized intensively by NINCDS extramural and intramural scientists to assess its promise of visualizing metabolism and function of the brain *in vivo*; this research may enhance the understanding of the nature of diabetes and its impact on cerebral function.

Veterans Administration (VA)

Mission

The Veterans Administration's (VA) primary mission is to administer veterans' law effectively and expeditiously with sympathetic understanding, and to exercise constructive leadership in veterans' affairs. To meet this goal, the VA has two major purposes: (1) the medical care and treatment of eligible veterans and (2) the administration of the various financial assistance programs for veterans and other eligible persons.

The VA's Department of Medicine and Surgery provides medical care and treatment to eligible beneficiaries and carries on an effective, comprehensive medical, health care

delivery, and rehabilitative engineering research program. Other VA activities include education for health care personnel to improve the supply of health manpower and a postgraduate continuing education program for its own physicians and other health care professionals.

The VA also encourages and promotes cooperative studies among several Veterans Administration medical centers. These examine diagnosis and treatment of various medical problems, including diabetes, its complications, and related disease entities. Moreover, the VA conducts collaborative research with other Federal agencies, including elements of the National Institutes of Health, as well as private proprietary and voluntary organizations with joint funding. In applying research results, the VA maintains a vigorous program of patient education, primarily in the area of hypertension and diabetes.

Achievements

Progress in Understanding the Relationship Between Diabetes and Blood Clotting

Clinical research into the factors that contribute to platelet aggregation in the diabetic is currently in progress. Eleven VA medical centers are collaborating in this effort to determine pathogenetic mechanisms and to evaluate the efficacy of various pharmaceutical agents in preventing this complication. The role of von Willebrand's Factor, growth hormone, high and low density lipoproteins, cholesterol, and prostaglandins are also being investigated.

From these studies, it is hoped that a better understanding of the pathologic process may be achieved, and appropriate therapeutic mechanisms developed to prevent abnormal aggregation and coagulation. This may help decrease vascular compromise and gangrene and, eventually, the need for therapeutic amputation in the diabetic population.

Clinical Investigation of Preventive Interventions in Coronary Artery Disease and Angina

The role of aspirin and other pharmacologic agents in the prevention of coronary artery disease and angina and the role of surgery in the treatment of stable and unstable angina are also being investigated in cooperative studies among several VA medical centers. The increased incidence of coronary artery disease among diabetics is well known. With data forthcoming from the studies, perhaps a more effective means of predicting those patients who will develop coronary artery disease can be found and appropriate therapeutic measures can be developed to prevent this complication entirely, or to lessen its severity where prevention is not possible.

Special Emphasis on Diabetes in Geriatric Research and Education

The VA has established a program of Geriatric Research and Education Clinical Centers. These centers are unique in that their purposes are to link clinical research to patient care in the area of geriatric medicine and to act as a conduit to facilitate the rapid and appropriate dissemination of research information to the clinician. Although not disease-oriented per se, each center has its individual approach to clinical research problems. For example, the Geriatric Research and Education Clinical Centers at the Palo Alto Veterans Administration Medical Center is focusing its activities upon various geriatric metabolic problems, including diabetes mellitus. Thus far, eight such centers have been established, all at academically affiliated VA medical centers. Five of the centers have had a total of 12 geriatric fellows appointed during FY 1979.

From such a collaboration of basic research and immediate clinical care applications, a more rapid application of research findings to ambulatory and bedside medicine is anticipated, with a better understanding of disease mechanisms, particularly in diabetes, as they operate in the aging patient.

Early Diagnosis and Treatment Education Courses Offered

There is an ongoing need for continued professional emphasis on early and timely diagnosis and newer methods of therapy in the control of diabetes and its complications. As part of the VA's Regional Medical Education Centers, a series of courses and workshops for professional staff has been held at various VA medical centers throughout the country. Drug Therapy, a 2-day course providing 12 hours of certified continuing education credit, was held for physicians and other allied health personnel, particularly pharmacists. Clinical Nutritional Advances was a 2-1/2 day seminar providing 18 hours of certified continuing education credit for physicians, nurses, and dietitians. Nutritional Biochemistry, a 3-1/2 day seminar providing 25 hours of certified continuing education credit, was held for physicians and dietitians. Geriatrics: VA Challenge of the 80's was a 2-1/2 day seminar-workshop program for chiefs of staff and others involved in implementing policy alternatives through assignment of resources, Geriatric Research and Educational Clinical Centers Directors, geriatric fellows, and legislators.

Patient Education Stressed Throughout the VA

The need for aggressive patient education has been recognized and met by an active program of instruction on diabetes in virtually all VA health care facilities under the auspices of the Nursing Services. Teaching materials have been developed at the local level for newly diagnosed and

poorly controlled diabetics and their families. These serve as adjuncts to the one-to-one teaching performed by both Nursing and Dietetic Services. A recent sample revealed that, in 22 VA medical centers, time devoted to patient education in diabetes was more than twice that devoted to any other activity in the category of disease management. In some centers, staffing includes a diabetes nurse whose only assignment is education of diabetic patients and their families.

Manpower Development and Professional Education

Manpower training in diabetes, both medical and paramedical, continues to be a major contribution which the VA makes on a national scale. During FY 1979, there were 5,000 more trainees within VA facilities than in the prior fiscal year. These 97,272 trainees received all or part of their training in VA health care facilities under the auspices of teaching affiliations with colleges, universities, community colleges, high schools, and other community organizations. These affiliations included 104 medical schools, 58 dental schools, 373 nursing schools, 74 schools of pharmacy, 181 schools of psychology, and 174 schools of social work. The trainees included 22,561 medical house staff, 19,550 medical students, 693 dental house staff, 1,031 dental students, 29,540 nursing students, 1,348 psychology trainees, 20,487 other health professions and occupations, and 807 administrative health personnel.

While there are no specific identifications of medical or dental residency programs that deal exclusively or primarily with categorical disease entities such as diabetes, residency programs in general internal medicine will involve the diagnosis and treatment of patients with diabetes to a large degree. Trainees enrolled in endocrinology programs will similarly be expected to evaluate and manage diabetic patients with complicated control problems. Obviously, a number of other disciplines and subspecialties—general surgery, vascular surgery, orthopedics, ophthalmology, hematology, infectious disease, immunology, neurology, cardiology, nephrology, psychiatry, and rehabilitation medicine, among others—may also participate in the diagnosis, treatment, and control of various complications associated with diabetes. In the specialty of general internal medicine, the VA devoted 2,454 man-years to 92 programs; in endocrinology, it devoted 72 man-years to 41 programs during FY 1979.

Health Care Facilities and Equipment

The VA continues to be heavily involved in the treatment of veterans with diabetes mellitus. At the end of FY 1979, the VA operated 172 medical centers with 87,551 beds, 92 nursing homes containing 8,357 beds, and 16 domiciliaries with 9,389 beds. The average daily hospital census of patients with the primary diagnosis of diabetes was 1,258 in FY 1979. During that fiscal year, there were a total of 72,444 diabetic patients discharged from VA medical centers (patients whose primary or associated diagnosis included diabetes). Diabetes represented 7.8 percent of all patients discharged during FY 1979, compared with 7.9 percent in the previous fiscal year. There were a total of 220 outpatient clinics in operation, with special Diabetic Clinics in 56 of them. In the remaining clinics, diabetic patients were seen and followed in the General Medicine or in the Endocrine Clinic.

As part of the Office of Research and Development, under the Chief Medical Director, the VA maintains an Office of Rehabilitative Engineering Research and Development which deals primarily with rehabilitation and prosthetics development, education, and patient training. It has a national reputation as one of the most innovative and imaginative organizations in the country dealing with rehabilitation and prosthetic problems. This organization has functioned in an active manner in disseminating information from the research laboratory to the physician, with specific relationship to patients and their prosthetic problems. Rehabilitation and patient education in the use of prostheses are of great importance to the diabetic amputee, whose disability frequently involves loss of a limb secondary to diabetic gangrene or vascular problems.

Social Adjustment and Mental Health Services

The Social Service units in each VA hospital deal specifically with patterns of behavior related to a particular disease process. In this context, they deal to a great extent with the patient with diabetes or its complications. They are frequently called in to help with family problems associated with the patient's admission and discharge. In addition, they become heavily involved in discharge planning and coordinate such post-discharge plans with other community agencies. They provide group and individual counseling of the veteran patient and act as a connection for the patient and family to community resources. Social adjustment and counseling groups also become intimately involved in the process of patient and family education, with respect to adjustment to the emotional, psychological, and financial demands of the patient's disease process.

National Center for Health Statistics (NCHS)

Mission

The National Center for Health Statistics (NCHS) conducts national studies, publishes results, and releases microdata tapes on diabetes epidemiology. Statistics concerning the prevalence, incidence, and distribution of diabetes with associated medical conditions and therapies are available

from interviews and examination study sources. Utilization patterns, multiple morbidity, and cost data for diabetic patients and others using health resources are available through studies of provider records, physician encounter forms, vital record follow-back questionnaires, and insurance records. The vital statistics system also provides data about mortality and its geographic distribution.

To carry out its mission, NCHS designs and operates national data collection systems, conducts research on statistical and survey methodology, and engages in cooperative endeavors both within the nation and internationally. Its present surveys and inventory programs are structured to provide diverse health statistics on (1) the extent and nature of illness and disability in the U.S. population and their impact on the national economy; (2) the determinants of health and well-being; (3) births, deaths, marriages, family growth, and divorces or other family dissolutions; (4) the availability of various health care resources (including professional personnel and treatment facilities); (5) the utilization of all types of health care facilities; and (6) health care costs and financing. In addition to its traditional emphasis on the prevalence of acute and chronic illnesses, and on infant and maternal morbidity and mortality patterns, NCHS has new legislative authority for developing guidelines on epidemiologic statistics and for initiating broad statistical activities concerning the effects of environmental, employment-related, social, and other health hazards on public health.

Achievements

Prevalence of Diabetes

The National Health Interview Survey and the National Health and Nutrition Examination Surveys, I and II, provide U.S. prevalence estimates of diabetes, both known and actual, by demographic and socioeconomic status variables. The National Health Interview Survey, which is a continuing nationwide household interview survey, is the principal instrument for collecting information about health status, focused primarily on the resultant impact and disability, as reported in household interviews. The National Health and Nutrition Examination Survey II, which performed standardized physical examinations on a representative sample of the U.S. adult population in 1976-80, employed the same set of National Health Interview Survey household interview questions and had the added advantage of furnishing measures of subjects' responses to oral glucose tolerance testing and more detailed questions relating to diabetes. With this information, the degree of probable understatement of the diabetes prevalence collected by medical history interview and questionnaire techniques can be estimated. The National Health and Nutrition Examination Survey II data base, when complete, will be the best source of nationally representative blood glucose measurements, and will make possible estimation of the "true" prevalence of low blood sugar and diabetes, as well as characteristics of diabetic patients. The 1976 National Health Interview Survey provided the most recent information on the use of insulin, hypoglycemic drugs, and diet for diabetic treatment.

Diabetes-Associated Mortality

NCHS is preparing microdata tapes containing multiple causes of death for all years from 1969 through 1976, using data collected through the Vital Statistics System of the Nation, a cooperative effort of NCHS with the states and localities. From this source, researchers will be able to detect diabetes mellitus when it is listed on the death certificate both as a contributing cause and the underlying cause of death.

Diabetes-Related Utilization of Health Care Services

Five nationwide surveys by NCHS provide utilization data on persons with diabetes and their utilization of health care facilities. The National Health Interview Survey asks respondents for information about visits to physicians and dentists, episodes of illness in hospitals and nursing homes (their occurrence, duration, and surgical procedures performed), and use of medication. The National Ambulatory Medical Care Survey annually samples physicans in office-based practices. In this survey, office visits made by ambulatory patients are studied for a 1-week reporting period each year. When completed, the National Ambulatory Medical Care Survey will be the best single source of information about multiple morbidity in an outpatient diabetic population of the United States.

The National Hospital Discharge Survey continuously samples the hospital records of all inpatients who have been discharged one or more times from U.S. hospitals having at least six beds, in order to present nationwide hospital utilization data. The National Nursing Home Survey was designed to afford information about long-term care facilities in the United States that provide some level of nursing care. The intent of this survey was to permit the study of their services, costs and charges, staff characteristics and qualifications, and residents' sociodemographic and health characteristics. These data afford the opportunity for studying multiple morbidity associated with diabetes, as well as the extent of utilization of nursing home services resulting therefrom. The National Medical Care Expenditure Survey is being conducted jointly by NCHS and the National Center for Health Services Research to collect information on American families' health care utilization, expenditures, and access; health conditions, disability, and perceived health status; and health insurance coverage during calendar year 1977. In this one-time panel survey, data have been drawn from a representative sample of households, as well as medical providers and health insurers or

employers. With this data epidemiologists will be able to examine the cost-benefit ratios associated with various diabetes detection and treatment regimens.

Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA)

Mission

The mission of the Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA) with respect to diabetes is to provide leadership, policies, and support in the Federal effort to reduce and, where possible, eliminate psychosocial and behavioral problems associated with diabetes. The responsibility for implementing these goals predominantly resides within the National Institute of Mental Health (NIMH) and includes activites to conduct, foster, and support basic research into the epidemiology, causes, prevention, diagnosis, and treatment of a broad spectrum of mental and emotional disorders. Much of this research is applicable to diabetes mellitus and the various disorders to which diabetes is a contributing factor (heart disease, vascular disease, blindness, crippling paralysis, impotence, nutrition, endocrine disorders, mineral metabolism, and related disorders).

The NIMH also conducts research in biochemistry of behavior; psychopharmacology; biomedical and behavioral aspects of stress and illness; psychological and sociological factors in coping, adaptation, and psychopathology; social and emotional development; and lifespan issues. It administers extramural programs of relevant research grants, training grants, and fellowships. It conducts collaborative programs and studies in biomedical and behavioral research, especially as they relate to diabetes, and collects, prepares, and disseminates information on research progress, and on diseases and programs within the Institute's general area of interest. Moreover, NIMH encourages, sponsors, and organizes meetings, conferences, and symposia to speed communication of scientific information.

To fulfill this mission, ADAMHA carried out or supported eight research projects and one training program relevant to diabetes or diabetes care during FY 1979. One of these projects was supported by the National Institute of Alcohol and Alcohol Abuse; all others were carried out or supported by the National Institute of Mental Health. NIMH, along with other cosponsors, also supported the recent national conferences on behavioral and psychosocial issues in diabetes.

Achievements

Coping with the Burden of Chronic Psychosocial Stress in Diabetes

As the range of factors believed to affect the biological and medical status of the diabetic person broadens, understanding of the burden that diabetes places on the patient's family has deepened. The burden of chronic, severe psychosocial stress for patient and family must be recognized to consider the full impact of diabetes. The stress comes from knowing that the patient may have a shortened lifespan or that severe complications may result in blindness, that the patient may suffer mutilation or major physical handicaps, or that insulin reactions or life-threatening medical crises related to ketoacidosis may occur. At best, the daily problems of monitoring and regulating diet, exercise, and medication cause family stress.

Several NIMH projects recognize the importance of coping skills and management of stress for diabetic persons and their families. Two projects, for example, are focusing on individual and family coping patterns and adaptation at diagnosis and during the period immediately following the onset of illness in the child. Family organization at the time of diagnosis and patterns of reorganization as they affect the adjustment of the child and other family members are being investigated in one study which approaches these aspects of diabetes from a psychosomatic perspective. Another project is approaching the study of diabetes from the perspective that juvenile diabetes is an example of the type of stress and challenge faced by most children in striving to establish their personal and social identity. Investigators are attempting to evaluate the conditions that contribute to maintaining an adaptive developmental course, including effective coping with the illness itself and effective functioning with regard to social relations, school, and extracurricular activities. Health attitudes and beliefs of medical personnel as influential factors on coping behaviors are also being studied.

Investigations of Stress Factors in Glucose Regulation

Recent research has shown that many factors control glucose regulation, the most prominent of which appears to be stress. Some of the effects of stress on diabetes management are being examined in a project involving metabolically labile (poor control) diabetics, diabetics whose illness has been under consistently good control, and nondiabetics. The study hypothesizes that there are significant individual differences in diabetic persons' biomedical responses to stress, and that these differences will systematically affect the ability to control diabetes metabolism.

Biomedical responses to three types of stress are being assessed—the stress of physical exercise; emotional, interpersonal stress; and emotional but noninterpersonal stress.

There are clinical approaches to the treatment of some labile diabetics that involve the assumption that poor control is due to interpersonal stress reactions stemming from certain intrafamilial conflicts and disturbed patterns of family interaction. This project hypothesizes, however, that for most diabetics there are many kinds of stressors that can cause control problems.

Although emotional stress, psychosocial factors, and family interaction patterns have all been thought to influence compliance and complications in the course of diabetes, there has been very little systematic study using a psychosocial-biological stress interaction model. This study is investigating whether the biologic and psychologic systems are interdependent, mutually influencing each other at all times. The study is collecting both biologic and psychologic data. For each of the experimental procedures, plasma epinephrine and norepinephrine, growth hormone, cortisol, glucagon, somatostatin, and glucose are being measured before, during, and after induction of different types of stress. Heart rate is being continuously recorded during procedures as an independent measure of arousal.

Some of the psychological variables being assessed include: overall psychiatric and behavioral status; affective states (e.g., depression), patterns of daily interaction, and family dynamics; knowledge of diabetes and skill in routines of diabetes management; stressful life events; and social supports as moderators of stress.

This project is a collaborative, intramural effort involving several laboratories within NIMH, the National Eye Institute, and the National Institute of Arthritis, Metabolism, and Digestive Diseases. A National Eye Institute investigator is conducting ophthalmologic examinations, and participants are being examined for signs of diabetes-related eye disease. The NIAMDD is overseeing and providing for patient care of the subjects while they are participating in the study at the NIH Clinical Center.

Evaluation of Risk Factors Associated with the Use of Alcohol by Diabetes Patients

Another research project involves the examination of the influence of acute and chronic ethanol administration on the pancreas and on various phases of glucose metabolism. Both normal and diabetic rats are studied. Additional investigations are undertaken employing pancreatic islet cells isolated from normal and diabetic animals in order to establish the possible direct effects of ethyl alcohol and acetaldehyde on pancreatic endocrine function. This project should contribute to the understanding of some of the risk factors involved in the use of alcohol by diabetics.

Examination of Sexual Complications of Diabetes

Sexual dysfunction is one of the possible complications of diabetes, and NIMH supports two research projects investigating this problem area. In one project, both psychologic and endocrinologic factors are being examined and compared among four groups—diabetic persons with and without sexual dysfunction and nondiabetic persons with and without sexual dysfunction. Responses to standard sex therapy are also being compared among diabetic and nondiabetic persons with sexual dysfunction. The second study focuses on the psychophysiologic aspects of sexual function, and diabetic males are one of the subject groups.

For male diabetics, fear of impotence as a complication of diabetes may lead to psychologically induced impotence. These projects aim to better understand the origins of diabetes-related organic impotence, to differentiate organic from psychologic impotence, and to improve treatment of impotence associated with diabetes.

Diabetes Training for Mental Health Specialists

NIMH is sponsoring a training program which attends to the diabetes-related psychosocial needs of elderly and minority diabetic persons. The program trains social work students to become competent mental health specialists capable of working with high-risk target populations, such as the lower socioeconomic black elderly with diabetes. Since high-risk populations are more apt to have difficulty managing diabetes and its attendant problems and are less apt to be able to effectively mobilize resources for dealing with the difficulties, such training programs are especially valuable.

National Conference on Behavioral and Psychosocial Issues in Diabetes

In spite of the well-recognized association between diabetes and behavioral and psychosocial factors, the scope of the problem is not known, and there has been little research on inter-relationships among various psychosocial factors. To encourage the identification and study of behavioral and psychosocial factors associated with diabetes and its complications, a national conference was held.

The conference, "Behavioral and Psychosocial Issues in Diabetes," was held in Madison, Wisconsin, in May 1979. It was sponsored by NIMH, NIAMDD, NICHD, NHLBI, NIA, and the National Diabetes Advisory Board. Leading diabetologists, behavioral scientists, and those who live with diabetes reviewed the emotional and psychosocial problems associated with diabetes and suggested ways to address the problems. The conference findings have been described in Chapter II of this report.

Center for Disease Control (CDC)

Mission

The Center for Disease Control's (CDC) diabetes control program, in partnership with states and other organizations and agencies, seeks to reduce the social and economic costs of diabetes by application of existing knowledge and traditional disease control techniques, including problem identification, appropriate and timely interventions, evaluation of results, application of new findings, dissemination of information, and coordination, cooperation, and communication between agencies/groups with parallel diabetes interests.

The program provides consultation and technical assistance to state and local diabetes control programs in the areas of epidemiology, surveillance, planning, evaluation, coordination, consensus-building, patient and professional education, and related activities. It collects, analyzes, publishes, and disseminates data relative to diabetes and promotes collaboration and exchange of information between states. It also plans, coordinates, and conducts meetings and conferences focusing on community-based control programs. Moreover, the program assesses, plans, coordinates, conducts, and evaluates training courses for state and locally based diabetes control personnel. Beyond this it promotes, advises, and maintains liaison with official, private, and voluntary agencies/groups for the purpose of fostering and improving efforts aimed at increasing the quality, availability, and effectiveness of existing diabetes services.

Achievements

Community-Based Diabetes Control Programs

Under the stewardship of the Center for Disease Control, 12 states are working cooperatively to conduct community-based diabetes control programs. In the first phase (planning) of a project, each state is required to collect and assess baseline morbidity, mortality, and care resource data; to establish a framework for improving coordination of community resources; and to develop a plan of action for improving control of diabetes to be implemented during the second (intervention) phase.

While the overall number of diabetics directly affected by these demonstration efforts remains relatively small in comparison with the estimated number of diabetics in this country, the potential benefits from conducting relatively few, but epidemiologically sound and rigorously evaluated, demonstration programs is enormous. For instance, the impact on costs can be significant, and the 6,000 patients directly exposed to community-based diabetic patient education courses in fiscal year 1979 will be followed to determine the program's effectiveness in reducing hospital days and costs of treatment. Similarly, professional education activities involving over 2,200 providers in fiscal year 1979 indirectly benefit many thousands of patients. The effect of these collaborative programs on the health status of diabetic populations will also be assessed.

Epidemiologic studies are another high priority. Rhode Island has amassed an impressive amount of useful information on ketoacidosis and on juvenile diabetes through its registry. These data have been the baseline for the formulation of specific activities in their respective areas. Both Rhode Island and Mississippi are continuing to investigate methods to improve pregnancy outcomes among overt diabetics as well as gestational diabetics.

Three states are addressing the issue of third-party payment for diabetic patient education in outpatient settings. These initiatives have resulted in the collaboration of a variety of interested parties, both public and private. Blue Cross/Blue Shield and other private insurers, Medicare, and Medicaid are also becoming increasingly involved with cost-containment initiatives in the project states. From this cooperation, a mutual understanding of the inherent factors with which each group must deal has emerged.

Department of Defense (DOD)

Mission

The Department of Defense (DOD) sponsors health care programs that provide the support necessary to maintain the combat readiness and effectiveness of the Federal uniformed services. DOD activities relating to diabetes are integrated within its operational health care functions.

DOD provides fully comprehensive health care to authorized beneficiaries. A wide variety of hospital and outpatient professional services in support of diabetic patient care are routinely available. These include general and highly specialized physician and nursing care, dietary instruction, physical therapy, podiatric care, pharmacy support, and social services.

DOD sponsors training programs in operational and clinical specialties for physicians as well as paramedical and other health science personnel. Education and training in diabetes are an integral part of all such programs.

Achievements

Provision of Medical Care

During 1979, DOD provided medical care to 9 million authorized beneficiaries. Approximately 10,000 full-time physicians have delivered primary care at 170 medical centers/hospitals and 300 medical clinics in the United States

and abroad. State-of-the-art health services, including ophthalmic photocoagulation and vitrectomy, renal dialysis, vascular surgery, and outpatient clinics specializing in diabetic care, have been available to diabetic patients within each medical region.

The Uniformed Services University of the Health Sciences, organized under DOD, is authorized to develop advanced degree programs in the various health sciences. During the past year, the School of Medicine has become fully operational, having accepted its fourth class and received accreditation from the liaison committee on medical education. While DOD does not currently administer or sponsor individual training programs in diabetes mellitus, such training is offered as part of the primary care clinical specialties. There are currently more than 2,600 resident physician trainees in the primary care specialties, including 350 in internal medicine. An additional 17 physicians are training at the subspecialty level in endocrinology-metabolism.

Research

In the area of biomedical research, DOD is authorized to support projects that are clearly and directly related to its mission. Therefore, DOD does not currently fund or administer major research programs in diabetes mellitus. However, DOD does sponsor a number of clinical research projects in diabetes-related areas which are limited in scope and relate primarily to patient care and teaching functions of military medical centers.

As an example, one current research activity addresses the problem of providing state-of-the-art care to a large diabetic patient population through outpatient facilities. Here computer technology (a comprehensive algorithm), a diabetes nurse educator, and two corps persons are utilized to maximize physician effectiveness. Additionally, computerization of diabetic patient records facilitates the record-keeping process and provides rapid data retrieval capabilities in support of both patient care and clinical research.

Food and Drug Administration (FDA)

Mission

The mission of the Food and Drug Administration (FDA) is to protect the public health as it may be impaired by drugs, food and food additives, medical devices, biological products, cosmetics, and radiation-emitting products. Drugs approved for use in diabetics must be shown to be safe, effective, and properly labeled. Batches of insulin are certified for strength, quantity, and purity. The FDA assures that foods available for diabetics are safe and wholesome, and that they meet established standards of identity, labeling, and packaging. The Agency also determines that devices used in the treatment of diabetes are safe and effective.

Achievements

Regulations Concerning Insulin Certification

Following a proposal and comment period, the FDA published regulations on September 25, 1979, that discontinue certification of all 80-unit (U-80) insulin products effective March 24, 1980. The U-40 and U-100 strength will continue to be available as over-the-counter drugs.

Regulations Concerning Special Dietary Food Labeling

The FDA published regulations in the fall of 1978 that revise label statements for special dietary food to be used in reducing or maintaining body weight or caloric intake, and for food to be used in the diet of diabetics. Nutrition-labeling information is to be included, and the conditions under which a food may be labeled as "low calorie" and "reduced calorie" are specified. The effective date for these regulations is July 1, 1980.

Health Care Financing Administration (HCFA)

Mission

The Health Care Financing Administration (HCFA) is a principal operating component of the Department of Health, Education, and Welfare. It places under one administration the oversight of the Medicare and Medicaid programs and related Federal medical care quality control.

Four major programs are directed by HCFA: Medicare, Medicaid, Quality Assurance, and Demonstration and Research. The Medicare program provides basic health benefits to recipients of Social Security and is funded through the Social Security Trust Fund. The Medicaid program, through matching grants to states, provides medical services to the needy and the medically needy. A focal point is established to carry out the quality assurance provisions of the Medicare and Medicaid programs and maternal and child health legislation of the Social Security Act, including the implementation of the Professional Standards Review Organization (PSRO) program and the End-Stage Renal Disease (ESRD) program. The Demonstration and Research program develops demonstration and research activities related to the above operating components including hospice programs.

Achievements

The Health Care Financing Administration directs both Medicare and Medicaid. These programs finance health care services for the elderly and disabled, and for those receiving welfare assistance. The extent to which these programs pay for diabetes-related services cannot be estimated since the program categorizes its clients by medical need rather than diagnostic category.

Medicaid

The Medicaid program is a national assistance program that reaches 23 million poor people, many of whom are also aged, blind, handicapped, or otherwise disabled. The program operates in every state but Arizona, and is administered by the states with costs shared by the Federal government. Although the states' shares vary, their average share of the total cost is 44 percent; the average Federal share is 56 percent.

By law, states are required to offer doctor, hospital, and skilled nursing home care; health screenings and followup treatment for children; laboratory and X-ray services; home health care services; family planning services; and rural health clinic services. Optional services provided by a state may include dental care, eyeglasses, clinic services, prescribed drugs, care in an intermediate care facility, and services by optometrists, podiatrists, and chiropractors.

Special programs and initiatives developed within Medicaid include the following:

- Early Periodic Screening, Diagnosis, and Treatment;
- Programs to improve the quality of long-term care for older persons in nursing homes, mental hospitals, and other care facilities, and to promote and improve noninstitutional care in the community for chronically ill, disabled, or aged persons; and
- The Quality Control Program, which assures that services go only to those eligible for them and that states do not make erroneous payments to providers (hospitals, nursing homes, and physicians), and which manages improved fraud and abuse control programs.

Medicare

The Medicare program is a Federal health insurance program for people who are 65 or older and covers health services in two parts. Younger persons can be eligible if they have been receiving disability benefits from Social Security for 24 consecutive months, if they need continuing dialysis for permanent kidney failure, or if they are preparing for a kidney transplant. Benefits of the program include hospital insurance (Part A) and medical insurance (Part B).

Claims for hospital services provided under Part A are handled by private insurance companies, called intermediaries, under contract to the government. Payment is made directly to the hospital, skilled nursing home, home health agency, or outpatient physical therapy facility. Claims for medical services provided under Part B are handled by the insurance carriers, and payment is made either to the supplier or to the beneficiary.

Professional Standards Review Organization (PSRO)

The Professional Standards Review Organization (PSRO) program supports a nationwide network of physician peer review organizations, the purpose of which is to assure that health care services delivered under Medicaid, Medicare, and the Maternal and Child Health Program are medically necessary, appropriate, and of acceptable quality, and that they are provided efficiently and economically. PSRO's are charged with:

- Assuring that health care services are of acceptable professional quality;
- Assuring appropriate utilization of health care facilities at the most economical level consistent with professional standards;
- Identifying quality and utilization problems in health care practices and working toward their improvement; and
- Attempting to obtain voluntary correction of inappropriate or unnecessary practices in hospitals. Approximately 55 PSRO's are also reviewing services provided in long-term care facilities.

PSRO's review hospital admissions, certify the necessity for continuing treatment in an inpatient facility, review other extended or costly treatment, conduct medical evaluation studies, review care profiles of facilities and practitioners, and review facility and practitioners' records.

Health Resources Administration (HRA)

Mission

The Health Resources Adminstration's (HRA) goal is to improve the health care system and the overall health care of the American people.

In pursuit of this goal, HRA administers programs designed to improve the distribution and quality of health care personnel and facilities. The Agency encourages innovative methods of developing and utilizing health personnel and facilities through program support administered by its bureaus.

Although HRA does not support disease-specific programs, it supports several training programs which are particularly relevant to diabetes control and reduction. These programs are administered by the Bureau of Health Professions for support of health professions development through the Educational Assistance Act of 1976 (P.L. 94-484) and other legislative authorities.

Assistance to health professions schools and students is provided to meet the cost of basic and postgraduate training programs in many health professions. The program seeks to

transfer knowledge gained through recent research into patient care as rapidly as possible in several fields, including diabetes, through continuing education and professional preparation. Although specific funding support is not identified for diabetes or other diseases, it is important to understand that knowledge of diabetes in health professions training for patient care is an important component of Bureau of Health Professions-supported programs.

Achievements

Training Programs for Nurse Practitioners

Nurse practitioners are registered nurses who have completed formal programs of study designed to prepare them to function in expanded nursing roles. They work in a variety of primary health care settings, serving mostly an ambulatory population. The services provided by nurse practitioners are not intended to supplant those provided by physicians, but rather to supplement them. Nurse practitioners function with the credential of individual licensure as registered nurses, fully accountable for their own practice.

Programs to prepare nurse practitioners are located throughout the country. The Professional Nurse Traineeship Program provides assistance for study at the graduate level for registered nurses who wish to continue their professional education in certain specified areas, including nurse practitioner training. Another program, the Nurse Practitioner Traineeship Program, provides assistance to registered nurses who are residents of and agree to practice in health shortage areas. Currently, there are approximately 14,000 nurse practitioners working and providing health care services. This number will probably continue to grow as employment opportunities increase, especially in the underserved rural and inner-city areas.

Improving the Availability of Health Care Personnel

The Area Health Education Center program addresses problems of geographic maldistribution and overspecialization of health professionals by fostering changes in the pattern of education and the education environment. The program provides funds to medical and osteopathic schools for the purpose of decentralizing education for medical and other health professions into primary medical manpower shortage areas and improving the coordination and use of existing resources.

The school of medicine or school of osteopathy responsible for the program must meet specific requirements. A school must provide that 10 percent of its undergraduate clinical education for medical students will be conducted in sites that are part of the center. In addition, the school must be responsible for a residency program in at least one center. Moreover, at least two other health professions schools, including dentistry (if there is a dental school at the contracting institution), must train students in center sites. There is a provision that 75 percent of the funds awarded to the school must be spent in the center.

From the other side of this partnership, the center must designate a specific geographic or medically underserved population to serve, assess the manpower needs of the service area, and have an advisory board which includes representatives of the community. Programmatically, the center must provide the sites for the training of the medical and other health professional students. It must provide support services including continuing education to National Health Service Corps personnel stationed in the service area.

Programs for Public Health Nutritionists Contribute to Resources for Diabetes Health Care

The public health nutritionist assesses community nutritional needs and plans, implements, and evaluates the nutritional component of health services. Advances in knowledge and technology, as well as in the number and type of programs designed for special groups, have created a demand for nutritionists with education and experience in specialized areas. Such specialties currently include maternal and child health (including work with the mentally retarded and the handicapped), geriatrics, chronic disease, and rehabilitation. Other areas of focus include adult health, migrant health, adolescent health care, and school and community health programs.

The Health Professions Educational Assistance Act of 1976 authorizes traineeship or student assistance grants to accredited schools of public health and other public or nonprofit institutions that provide graduate or specialized training in public health, including nutrition. Of 2,110 students actually receiving funds through formula grants for traineeships awarded in 1978, 131 were specializing in nutrition or dietetics. Section 792 of the Public Health Service Act provides for project grants to enrich a broad range of public health curricula, including nutrition, in accredited schools of public health and other educational institutions offering graduate level degrees. In 1978, seven grants at a level of $329,424 were awarded under Section 792 to programs in nutrition or dietetics located in schools of public health. In 1979, seven grants for $353,930 were awarded.

National Health Service Corps Scholarship funds became available to train public health nutritionists in 1977-78. Eighteen students were awarded a total of $71,624 that year.

Health Services Administration (HSA)

Mission

Several Health Services Administration (HSA) subprograms conduct activities that are relevant to diabetes. The missions of these programs are presented separately.

Bureau of Community Health Services

The goal of the Bureau of Community Health Services is to assure the availability and accessibility of adequate health care for all citizens. In particular, they are concerned with the development and establishment of health care delivery capacity in medically underserved rural and urban areas. The Bureau does not single out diabetes mellitus as a major area of program emphasis or reporting; however, persons with diabetes are provided care within the context of this Bureau's overall health service delivery efforts.

Indian Health Service

The Indian Health Service is responsible for providing comprehensive health care to American Indians and Alaska Natives. Diabetes mellitus has become a major health problem among American Indians. The disease and its complications are more common among most Indian tribes than in the general population.

Bureau of Medical Services

The Department of Health, Education, and Welfare has a legislative mandate to provide direct health care services to specified beneficiaries under the provisions of the Public Health Service Act and the Dependents' Medical Care Act. This responsibility is discharged, in part, through the Bureau of Medical Services of the HSA and, within the Bureau, through its Division of Hospitals and Clinics and the Division of Federal Employee Occupational Health. The Division of Federal Employee Occupational Health contracts with Federal agencies to provide limited health care services to their employees. The program authority of the Bureau's Division of Emergency Medical Services does not encompass the direct delivery of health care services.

The Division of Hospitals and Clinics provides comprehensive health care services to American seafarers, active-duty members of the U.S. Coast Guard, members of the National Oceanic and Atmospheric Administration, and active-duty commissioned officers of the U.S. Public Health Service. Services may also be provided to retired members of the uniformed services under the authority of the Dependent's Medical Care Act, and to selected community residents.

Achievements

Bureau of Community Health Services Provides Care to Diabetes Patients

The Crippled Children's Program is the only program for which statistical data related to diabetes are reported. The latest data available indicate that 1,565 patients with diabetes were provided care by the Crippled Children's Program in 1976. This represents about 0.2 percent of the total Crippled Children's caseload.

Despite the lack of formally organized diabetes activities, most of the Bureau's other programs bear some relationship to diabetes. Urine analysis for sugar is a part of routine health assessment in many projects, and some also provide glucose tolerance tests. In addition to screening activities, followup services, counseling, and education services are often provided. Diabetes is considered a high-risk condition during pregnancy, and care is provided through the Maternity and Infant Care projects and the Maternal and Child Health programs.

Indian Health Service Develops Model Diabetes Care Projects

In FY 1979, the Indian Health Service received $925,000 to begin five model diabetes care projects. These are being developed in cooperation with the National Institutes of Health and the Center for Disease Control. The sites have been selected to represent the scope of Indian Health Service facilities and their setting so that experience gained in the model projects would have the widest possible applicability. The project sites are Ft. Totten, North Dakota; Winnebago, Nebraska; Claremore, Oklahoma; Albuquerque, New Mexico; and Sacaton, Arizona. Teams of health care professionals have been recruited, including physicians, community health nurses, physician's assistants, nutritionists, and lab technicians. Personnel have been sent for short-term training in diabetes and returned to their facilities to adapt the ideas they have learned into their own settings.

Information gained from the NIH studies of diabetes among the Pima Indians has provided a great deal of basic information about the disease and its complications. The CDC has assigned a Public Health Advisor to assist in the administration of the Indian Health Service program. The National Diabetes Information Clearinghouse has assisted in the development of a diet manual using foods common to Southwestern Indians. The Department of Agriculture's Extension Service has provided the support for instructing patients in the use of commonly available foods. Cooperation has been enlisted from tribal organizations in order to promote public education about diabetes.

Every effort has been made to use innovative approaches and develop culturally relevant diabetes and education programs,

with services to patients begun during FY 1979. The first phase of the program involves an examination of known diabetics, assessing complications, and designing followup plans to meet the patients' specific needs.

In cooperation with NIH, plans have been made for the development of in-service education for all staff at the model project sites using personnel from the Diabetes Research and Training Centers to provide the training. Future plans include the introduction of a computerized patient registry, which will facilitate program evaluation.

In the development of the five model care projects, Indian Health Service health care professionals have been sent for short-term training in diabetes at the Grady Hospital in Atlanta, the Diabetes Education Center in Minneapolis, and the Diabetes Research and Training Centers in Michigan. CDC provided consultation from a nurse educator. Plans call for the development of extensive in-service training in diabetes utilizing the resources of the Diabetes Research and Training Centers.

Heart disease has become a more frequent complication of diabetes than was seen in the past. It appears to be a particular problem in Oklahoma. A stress testing capability has been developed at the Claremore Indian Hospital to assess this complication of diabetes. Certain minor modifications of existing facilities have been made in order to improve patient flow and to provide space to see patients.

Although no mental health professionals were recruited for the Indian Health Service Diabetes Project, the attempt to develop culturally relevant approaches to the problem represents initiatives aimed at improving the social adjustment of the diabetic patient. Two examples are the Southwestern Indian foods diet manual and the health care providers' use of interpreters or native languages to reach patients. Community health nurses are making home visits to try to incorporate the family into the health care program.

Patient education is an integral part of the health services of the Model Diabetes Project. The prevalence of the disease is extraordinarily high in Indian groups and public education is extremely important. Several tribal resources have contracts with the Indian Health Service to develop a community awareness program in diabetes. On one reservation, district dinners have been held with a demonstration diabetic meal followed by presentations on diabetes and question-and-answer sessions. The turnout for these demonstrations has been very gratifying. Tribal organizations have focused on a number of different public education methods. Diabetes education in the schools is under development in some reservation sites. Other organizations have felt that techniques such as poster campaigns, booths at health fairs, and workshops would be helpful to increase the public's understanding of diabetes.

Evaluating the impact of the Indian Health Service program and assuring its quality have been important concerns from the outset. Using the Indian Health Service facilities, a patient registry is being developed which will allow a computerized data base to be collected on patients, and certain parameters can be followed on a long-term basis. This data system will allow various audits to be performed assuring that periodic surveillance and immunizations will be performed.

Bureau of Medical Services Provides Diabetes Patient Care

The Division of Federal Employee Occupational Health operates 154 clinics in Federal installations across the country. Health care services are provided by the Division of Hospitals and Clinics through 9 hospitals and 300 contract physicians, dentists, and hospitals located throughout the United States. This major system constitutes a nationwide network within the Department of Health, Education, and Welfare for delivery of comprehensive health care services, for training, and for research. Funds for clinical research studies are distributed through the Central Clinical Investigations Committee, a formally constituted body of the Division of Hospitals and Clinics. This committee is also responsible for monitoring and evaluating research programs within the Division. During fiscal year 1979, the Division of Hospitals and Clinics funds allocated for clinical research totalled $250,000, and approximately $61,891 was used for research associated with diabetes.

While it is known that all of the U.S. Public Health Service hospitals and clinics treat persons with diabetes, precise data regarding the number and extent of services rendered to people with diseases or conditions in these diagnostic categories on an outpatient basis cannot be obtained at this time. For fiscal year 1978, of the 32,982 discharges from Public Health Service hospitals, in 3,993 instances one or more of the discharge diagnoses were conditions associated with diabetes. Approximately 79,882 patient-days were utilized by this group at an estimated cost of $13.8 million, based on an average inpatient-day cost of $173. There were 35,355 discharges from Public Health Service hospitals in fiscal year 1979. During the first 6 months of fiscal year 1979, in 2,070 instances, one or more of the discharge diagnoses were conditions associated with diabetes. Annualized, it is estimated that approximately 78,960 patient-days were utilized by this group in fiscal year 1979 at an estimated cost of $13.9 million, based on an average inpatient-day cost of $176.

Diabetes-Endocrinology Research Center

The Public Health Service Hospital in Seattle, Washington, is cooperating with the Diabetes-Endocrinology Research Center of the University of Washington. The center is 1 of 11 diabetes centers supported by the NIAMDD in the

United States and provides research-related services to over 50 affiliated investigators from 20 University of Washington departments. The Hospital has renovated facilities for use by University of Washington investigators, and these highly skilled specialists enhance the Hospital's ability to provide diabetes patient care. Moreover, the investigators benefit from access to special study populations being served by the Hospital.

Hospital Participates in Diabetes Research

Much of the research currently under way at the Public Health Service Hospital in Carville, Louisiana, is related to immobile and sensitive limbs. This work has direct implication for contributing to the development of improved techniques in the treatment of diabetes. Potentially, the multiple facilities of the Division of Hospitals and Clinics could be used to study, develop, and/or apply research findings and other new methods and techniques in the treatment of diabetes, leading to the improvement of the delivery of services to this diagnostic group.

Department of Agriculture (USDA)

Mission

The mission of the Department of Agriculture (USDA) is to provide a safe, continuous, and reliable supply of wholesome food to the American consumer, and, when possible, to populations abroad. It is within the area of nutrition research that the work of the USDA has particular relevance for diabetes mellitus. In addition to nutrition research, the Cooperative Extension Service contributes to the overall thrust for the control of diabetes through nutrition education programs. USDA nutrition research and education programs contribute to the control of diabetes through both basic research and efforts to encourage preventive health measures.

Achievements

Emphasizing Nutrition Education in Diabetes Control

Cooperative Extension Service traditionally has directed nutrition education toward a healthy population. The basic concept has been to enhance the diets of families by improving:

- Their skills in fundamental home management activities including food preservation, sanitation, and preparation; and
- Their knowledge of the basic concepts in nutrition, thereby promoting changed attitudes related to food in order to improve dietary practices.

Recognizing that a preventive approach is desirable, the Cooperative Extension Service has recently placed emphasis on helping clients to improve their quality of life through sound nutrition concepts. One area of nutrition education that relates directly to the control of diabetes is weight control. Programs to improve weight control are evident in practically all of the USDA's state programs. Although the exact cause of diabetes still remains uncertain, there is ample evidence to indicate that obesity plays a considerable role in the incidence of maturity-onset diabetes mellitus, and these programs address this problem by providing diabetes-related educational materials.

USDA Basic Nutrition Research

The USDA supports a variety of basic studies in nutrition, and some of these are directly related to diabetes. In particular, USDA research on dietary carbohydrates and their metabolism as well as basic and clinical studies of glucose tolerance are especially relevant.

In the area of basic research, projects in the Carbohydrate Nutrition Laboratory, Nutrition Institute, involve the effects of various dietary sugars, fiber, and pattern of food intake on parameters related to glucose tolerance. These parameters include insulin sensitivity of adipose tissue, insulin response to test meals, and insulin/glucagon ratios in both normal and carbohydrate-sensitive humans.

The Vitamin and Mineral Nutrition Laboratory, Nutrition Institute, has continuing research projects to determine forms and bioavailability of chromium and natural materials, and requirements and modes of action of chromium. Evidence has been obtained that suggests that adequate dietary chromium is required for a normal tissue response to insulin.

IV. Plans
for the Future

The DMCC participates in planning future diabetes activities in a very important way. While each of the member organizations is responsible for developing its own program plans and new initiatives, the DMCC provides the mechanism for coordinating those plans, avoiding duplication, and developing a consensus on what will be the most rewarding directions to pursue in the future. Through the DMCC's ongoing information exchange, the members are made aware of areas in which current efforts are insufficient, in which new research opportunities exist, in which new research findings warrant programs to speed their application, in methods of program implementation that have proven successful, and in pitfalls to be avoided.

The DMCC provides the opportunity for member agencies to view all Federal diabetes activities with a strong sense of how the individual agency's programs fit into the whole. The DMCC is very conscious of its role in planning and has undertaken a variety of activities in this realm. One of these activities is the development of a data base on all diabetes activities, which is reflected in this report. Through this inventory of projects and programs, the members are better able to identify areas that require further attention, or areas that may be already fully covered and do not merit future expansion.

In addition to providing this overview, the DMCC undertakes special activities which it feels are needed to improve planning. For instance, a recent meeting was devoted to examining program evaluation methodologies, case histories, and the outcome of various evaluation studies of Federal health professional education programs. The thrust of the seminar was to allow the members to examine methods used in the education field with the goal of identifying useful evaluation tools which could be applied in other areas.

In other special projects, the DMCC has frequently shared information concerning the kinds of planning processes used by the member organizations and details of their plans for the future. This allows the members to review their plans with a knowledge of the overall Federal effort.

Of course, the DMCC itself does not implement programs; its member organizations do. But what is crucial is that the member organizations can plan for the future with a firm foundation based on a comprehensive view. This knowledge improves program planning throughout the government sector and much increases opportunities for cooperative undertakings.

The following paragraphs highlight some of the diabetes activities planned for implementation in FY 1980. They are by no means a comprehensive listing of all planned diabetes activities; nevertheless, the member organizations have suggested these descriptions as examples of the direction in which they intend to move during the coming year. It is important to note that these directions span the spectrum of programs, from fundamental research in biomedical processes to programs of education, demonstration, and control. It is this comprehensive approach, an appropriate balance of research, education, and services programs, that the DMCC has sought to foster.

NIAMDD Plans Projects To Build on Achieved Progress

As detailed in other sections of this report, significant progress has recently been made in expanding and coordinating research, manpower development, and information programs on diabetes. Significant scientific advances have been made through NIAMDD-supported, diabetes-related research that have an impact not only on our understanding and treatment of diabetes but also on a much broader range of noncategorical areas. For example, these advances include:

- An increased understanding of the mechanism by which insulin regulates cellular glucose metabolism through new insights into membrane receptor dynamics, membrane transduction and transport systems, and intracellular processes. These advances promise progress not only in understanding and treatment of certain types of diabetes but also form the basis upon which the molecular biology of the mechanism of action of a variety of peptide hormones may be unraveled.
- New knowledge regarding the etiologies of insulin-dependent and non-insulin-dependent forms of diabetes, particularly genetic heterogeneity and the role of immunologic and viral factors.
- Advances in gene isolation, nucleotide sequencing, and recombinant DNA technology that hold great promise for improved understanding of the genetic basis for diabetes, for identifying abnormalities causing various forms of diabetes, and for synthesizing insulin.
- The ability, in the rat, to transplant pancreatic islet cells across genetic lines without immunologic rejection and the consequent reversal of diabetes in these animals.
- The development of improved devices for delivering insulin to the body and the consequent potential for better regulation of glucose metabolism in the insulin-dependent diabetic patient to a degree heretofore not achievable.

Continued support of research in these as well as numerous other areas where new opportunities and needs can be identified will be provided by the diabetes programs of the NIAMDD.

NIAMDD Plans To Implement Recommendations of the National Conference on Diabetes

The recommendations of the October 1979 National Conference on Diabetes: Current Status and Future Directions will provide valuable guidance in the development of future directions for the Institute's diabetes programs. Some specific areas in which new or continued emphasis is anticipated include:

- **Research.** During the coming year, the NIAMDD will continue to give highest priority to support for investigator-initiated projects spanning the range of fundamental and clinical research related to diabetes and its complications. Specific areas of emphasis will include: regulation of hormone synthesis, secretion, and action; etiology including genetic, immunologic, and viral factors; pancreatic transplantation and insulin delivery systems (artificial devices) for improved management of diabetes; nutrition and obesity; diabetic complications, especially renal and microvascular lesions; diagnosis and treatment; and areas of behavioral research related specifically to the psychosocial aspects of diabetes. In light of both the potential research and therapeutic significance of insulin delivery systems, it is anticipated that an expansion of contract support for epidemiologic and public health studies will be necessary to translate basic clinical research findings into a better understanding of the natural history of diabetes, upon which improved clinical management and public health intervention programs can be based. This will be coordinated through the continuing activities of the National Diabetes Data Group.

- **Centers.** During the coming year, the Institute will continue to support the development of both Diabetes-Endocrinology Research Centers and multipurpose Diabetes Research and Training Centers. In addition, planning for an evaluation of center programs will be initiated in order to begin to assess the progress and accomplishments of these activities. It is anticipated that the information obtained through this evaluation study will provide a basis for the future development and evolution of responsive and effective center initiatives.

- **Clinical Trials.** Initiation of a clinical trial to study the relationship between the degree of control of blood glucose and the development of the chronic complications of diabetes has been temporarily postponed in order to enable the Program to assess the potential for capitalizing on recent advances in the development of insulin delivery systems and, if feasible, to incorporate suitable devices into the trial design. Planning for this trial, which will address perhaps the most significant clinical issue in diabetes, therefore remains a very high priority within the Institute.

- **Training and Career Development.** The Institute will continue to support a wide range of specialized training, fellowship, and research career awards in diabetes and related areas of endocrinology and metabolism. This has been and will remain a high priority in order to ensure the continued availability of research expertise in requisite scientific disciplines.

- **Information Programs.** Through the National Diabetes Information Clearinghouse, the Institute will continue to support workshops and conferences designed to provide a state-of-the-art assessment in appropriate areas of diabetes-related research. Specific sessions which are now anticipated during the coming year include: (1) a series of meetings to assess recent progress in the development of portable insulin delivery systems and devices for home monitoring of blood glucose, as these advances relate to defining the relationship between blood glucose control and development of the chronic complications of diabetes; (2) a workshop to evaluate the needs and opportunities for research related to the chlorpropamide-alcohol flush reaction; and (3) a conference on recent technological advances related to the development of glucose sensors. In addition, ongoing Clearinghouse activities will be continued to promote the development and dissemination of educational materials related to diabetes and its complications.

ADAMHA To Further Emphasize the Study of Psychosocial Factors in Diabetes

The National Institute of Mental Health (NIMH), one of the three Institutes of the Alcohol, Drug Abuse, and Mental Health Administration, has increasingly recognized the role of behavioral and psychosocial factors in diabetes and diabetes care. NIMH plans to continue to address the interdependency of psychosocial factors and physical health and to continue to stress inter-Institute cooperation.

Several NIH Institutes and NIMH also issued a 1979 joint program announcement inviting applications for research project grants in the area of behavioral studies related to diabetes. The program announcement will be reissued in 1980.

Eight New Diabetes Control Projects Planned by CDC

Fiscal year 1980 will see the addition of 8 new project states for a total of 20 Center for Disease Control Demonstration Project states. Information and experience gained from all the intervention projects will be coupled with the results from epidemiologic studies and other project activities to develop specific guidelines and recommendations for

community-based diabetes control programs nationwide. Such programs involve patient and professional education, diabetes pregnancy screening and followup, cost containment initiatives, third-party reimbursement practices, diabetes morbidity and mortality surveillance reporting, and a variety of other activities benefiting from the experience, interaction, and input of many other agencies and organizations. In fiscal year 1981, CDC plans to concentrate its resources and efforts on consolidating information and experiences gained from the 20 states and promoting discussions with other agencies and organizations before expanding to a comprehensive, nationwide program. Careful evaluation and sharing of what is learned by CDC in partnership with the states and other organizations will result in a strengthening and improvement of the health care system, the improved utilization of existing resources, and a concomitant increase in communication and collaboration of all concerned.

NICHD Plans To Stress Diabetes-Related Investigations and Begin Special Emphasis Research Career Awards in Diabetes

The National Institute of Child Health and Human Development (NICHD) will continue to emphasize research devoted to the prevention of diabetes mellitus and/or its sequelae. In particular, research will be encouraged on the following topics:

- Development of control of carbohydrate metabolism;
- Developmental endocrinology;
- Gestational diabetes;
- Infant mortality, congenital defects, and perinatal morbidity in infants of diabetic mothers;
- Ascertainment of risk factors in infancy and childhood for Type I and Type II diabetes mellitus later in life;
- Influence of feeding and weaning practices on development of obesity and insulin resistance in infancy and childhood;
- Influence of oral contraceptives on risk of glucose intolerance;
- Genetic and immunological aspects of Type I and Type II diabetes mellitus; and
- Psychosocial aspects of diabetes in childhood.

The NICHD is planning a conference in FY 1980 that deals with diabetes-related areas. Entitled "Food, Human Evolution, Health and Disease," the conference will explore evolutionary aspects of man's diet, and the effects on the human genome of the selective pressure exerted by man's nutritional environment.

The Institute expects in FY 1980 to fund several Special Emphasis Research Career Awards in endocrinological and metabolic aspects of diabetes during pregnancy and infancy. Obstetricians, neonatologists, and pediatricians will be the recipients of these new career development awards.

The NICHD is expanding its program on nutritional antecedents of disease later in life, with a special emphasis on certain aspects of obesity research, including: the development of insulin resistance; cerebral control of food intake; psychosocial determinants of excessive food intake, and subsequent obesity; feeding and weaning practices in early life and their effects on carbohydrate metabolism and energy balance; and development of predictors of obesity and insulin resistance later in life (including biochemical and enzymatic profiles of populations of fat cells).

DOD Strives To Apply Research To Patient Care Practices

During the past year, two major conferences aimed at updating Department of Defense (DOD) physician knowledge in the field of diabetes mellitus were held. The Society of Air Force Physicians, in conjunction with the American College of Physicians, presented a 1-1/2-day seminar on diabetic care in San Antonio, Texas, in March 1979, which attracted 250 internists. In September 1979, a similar program was sponsored by the Naval Regional Medical Center, Portsmouth, Virginia. It is anticipated that a third program, sponsored by the Uniformed Services University of the Health Sciences, will be held in Bethesda, Maryland, in May or June 1981. The emphasis of such programs is on translational activities, i.e., the incorporation of newer research developments into patient care practices.

Dental Complications of Diabetes Will Receive Continuing Emphasis in NIDR Progams

Since some of the National Institute of Dental Research (NIDR) scientific approaches already initiated seem to offer unusual promise both in the general field of diabetes and in the area of dental complications, these efforts will be developed further. Early in FY 1980, the Institute will fund a new grant project to systematically investigate periodontal disease in juvenile diabetic patients. This project will correlate the clinical periodontal status of each individual with protective neutrophil functions and with the general competence of the immune system. The investigators will also determine whether the periodontal microflora in diabetes is unique.

The extramural staff has scheduled a 1-day workshop on the periodontal complications of diabetes mellitus at the April 15, 1980, meeting of the Institute's advisory subcommittee on periodontal disease. This workshop is expected

to set the stage for the development of a larger conference or symposium. It is hoped that these activities will lead to definitive plans for future research and will encourage members of the scientific community to develop research related to the oral complications of diabetes.

New Food Labeling Regulations To Be Proposed by the FDA

The Food and Drug Administration, in a cooperative venture with the Department of Agriculture and the Federal Trade Commission's Bureau of Consumer Protection, has undertaken a comprehensive review of current food labeling laws and regulations. A series of public hearings was held in the fall of 1978 to discuss issues such as ingredient labeling, nutrition labeling, and imitation foods. The Agency will propose to change several food-labeling regulations, for example, those concerning sugars in foods as part of nutrition labeling.

NEI To Stress Research on Eye Complications of Diabetes

During 1980, the National Eye Institute (NEI) will continue to support development of a science base related to the causes and treatment of diabetes-induced ocular complications, primarily through investigator-initiated research projects. Research in the following areas will be encouraged: (1) determining the etiology of neovascularization, (2) utilizing animal models and human tissues to elucidate the biochemical and physiological mechanisms underlying ocular complications of diabetes, and (3) developing noninvasive methods of measuring blood flow. Transfer of knowledge from the various clinical trials to the practicing physician will also be a major priority.

A task force to discuss the research needs relevant to the clinical and fundamental problems of diabetic retinopathy will be held in the winter of 1980. In addition, NEI plans to implement the recommendations of the National Conference on Diabetes (October 1979) and of the updated National Advisory Eye Council's Vision Research Plan.

NHLBI Sees Expanding Opportunities in Research Concerning Heart, Lung, and Blood Complications of Diabetes

The National Heart, Lung, and Blood Institute has achieved great momentum in the improvement of the Nation's health in cardiovascular, pulmonary, and blood diseases. New information and research opportunities have, as a consequence of these successes, unfolded in programs which relate to the cardiovascular aspects of diabetes.

A number of opportunities exist for future research, including:

- Studies of the effect of diabetes on the cerebral vasculature;
- Pathogenetic enhancement of plaque formation in atherosclerosis by diabetes;
- Studies on the contribution of diabetes to congestive heart failure;
- The effect of diabetes on major mechanisms involved in the development of hypertension;
- A program of small supplementary grants to add diabetic variables to existing programs in cardiovascular disease;
- The effect of glucose and insulin on lung development and surfactant production;
- The effect of hemoglobin glycosolation on hemoglobin function; and
- Studies on the interrelationships of obesity and glucose intolerance and hypertension.

NIAID Plans Diabetes-Related Workshop

In the coming year, the National Institute of Allergy and Infectious Diseases will continue its ongoing research support related to diabetes. In a special effort, the Institute plans to collaborate with NIAMDD on a workshop in new opportunities for research in the immunology of diabetes. The workshop will focus on diabetology, immunology, virology, and epidemiology.

New Emphasis on Environmental Factors in Diabetes Planned by NIEHS

The National Institute of Environmental Health Sciences has announced in the NIH Guide for Grants and Contracts in 1980 a new emphasis on diabetes and diabetes-related research. The Institute's primary interest focuses on acute and chronic toxicological effects of environmental chemicals on the pancreas with reference to acinar cell cytotoxicity, effects leading to duct obstruction, and cancer induction and studies on the basic mechanisms of toxic injury to pancreatic cells using animal models. The development of more sensitive and specific methods to detect "subclinical" degrees of acute acinar cell injury and focal duct obstruction is stressed. Studies concerning population groups that may be at risk from exposures to known pancreatoxic agents, and prospective studies to detect glycosuria or abnormal glucose tolerance in human populations considered to be at risk for exposure to any toxic agents suspected of affecting islet cells, are also of special interest.

VA Continues To Encourage Research Through Career Development Awards

For several years, the Office of Research and Development within the Veterans Administration (VA) has carried out a Medical Research Career Development Program. This program provides a career progression from beginning research assignments to a full career in academic medicine and research for well-qualified clinical health professionals at the doctoral level. The various steps in this program include the Associate Investigator and the Senior Medical Investigator levels.

A review of titles of proposed areas of investigation by recently accepted applicants for the career development program provide an indication of research relative to diabetes that will soon be under way within the VA. Recently funded projects in this program include (1) Impact of Hemodiafiltration on Hemodialysis-Carbohydrate and Lipid Abnormalities of Patients on Maintenance Dialysis, and (2) Prostaglandin E and Diabetic Ketoacidosis.

Recently approved but not-yet-funded projects in this program include (1) Vasoregulatory Systems in Diabetes, (2) Metabolic Studies in Diabetes and Hypertension, and (3) Effect of Insulin, Glucose, and Insulin-like Growth Factors on Collagen Metabolism by Human Endothelial Cells. Each of these will be funded over a period of several years.

V. Overview
of FY 1979 Federal Diabetes-Related Activities

An appendix to this report lists all diabetes-related projects funded by the Federal Government during FY 1979. The listings are organized by category of activity and sponsoring organization and are intended for specialized uses. Funding levels reported may be estimates if exact fiscal data are not readily available. If only a portion of a reported activity is relevant to diabetes, the appropriate portion of the total funding is indicated wherever possible.

Detailed funding information is summarized in the following tables and charts. Table 1 indicates total FY 1979 funding by category of activity. Table 2 presents funding totals by category and by sponsoring organization. For each category of activity, bar graphs depicting total funding by sponsoring organization are provided. These are intended to allow the reader to compare the respective contributions of different funding information over a 4-year period and allow the reader to trace changes in funding levels over time.

For this compilation, each discrete project has been assigned to an activity category. The categories used in this report are as follows:

A. Epidemiology (See B 21)

B. Research

1. Resources
2. Etiologic Factors including genetic, immunologic, infectious, and other factors relating to the cause of diabetes
3. Nutrition, Exercise, and Obesity
4. Hormones
5. Intermediary Carbohydrate and Protein Metabolism
6. Transplantation and Artificial Devices
7. Nonhormonal Blood Factors, Platelets, and Coagulation
8. Lipid Metabolism, Lipoproteins, Cholesterol, and Triglycerides
9. Pancreas and Islet Cell Studies
10. Microangiopathy
11. Macroangiopathy
12. Heart and Circulation
13. Central and Peripheral Nervous System
14. Nephropathy
15. Ocular Complications
16. Dental Complications
17. Infections
18. Pregnancy and Perinatal Problems
19. Psychosocial and Behavioral Problems
20. Pharmacologic Agents
21. Epidemiology
22. Health Services

C. Health Care Delivery

1. Health Care Facilities and Equipment
2. Health Care Services
3. Social Adjustment and Mental Health Services
4. Public Education
5. Patient Education
6. Quality Assurance
7. Health Care Financing
8. Health Planning and Evaluation

D. Manpower Development and Professional Education

1. General
2. Career Awards
3. Fellowships and Training Programs

E. Multidisciplinary Programs

1. Diabetes Research Centers
2. Diabetes Research and Training Centers
3. General Clinical Research Centers
4. Other Multidisciplinary Programs

F. Workshops, Conferences, and Publications

G. Unclassified

Project data are also presented by sponsoring organization. In FY 1979 the organizations reporting diabetes-related activities are the following:

ADAMHA/ NIMH	Alcohol, Drug Abuse, and Mental Health Administration/National Institute of Mental Health
BCHS	Bureau of Community Health Services
BHM	Bureau of Health Manpower
CDC	Center for Disease Control
DOD	Department of Defense
DMCC	Diabetes Mellitus Coordinating Committee
DRR	Division of Research Resources

FDA	Food and Drug Administration
HCFA	Health Care Financing Administration
HRA	Health Resources Administration
HSA	Health Services Administration
IHS	Indian Health Service
NCHSR	National Center for Health Services Research
NCHS	National Center for Health Statistics
NEI	National Eye Institute
NHLBI	National Heart, Lung, and Blood Institute
NIAID	National Institute of Allergy and Infectious Diseases
NIAMDD	National Institute of Arthritis, Metabolism, and Digestive Diseases
NICHD	National Institute of Child Health and Human Development
NIDR	National Institute of Dental Research
NIEHS	National Institute of Environmental Health Sciences
NIGMS	National Institute of General Medical Sciences
NIH	National Institutes of Health
NINCDS	National Institute of Neurological and Communicative Disorders and Stroke
NIA	National Institute on Aging
NSF	National Science Foundation
PHS	Public Health Service
SSA	Social Security Administration
USDA	Department of Agriculture
VA	Veterans Administration

Not all organizations sponsor activities in every category, and thus the graphs for individual categories include only those organizations reporting specific activities within that category. The graphs indicate the relative contributions of different Federal organizations to a particular category of diabetes-related activity.

Table 1.—Total Federal diabetes-related activities by diabetes subtopics: FY 1979

Diabetes Subtopic	Funds
A. Epidemiology (see B 21)	
B. Research	
1. Resources	$ 2,369,451
2. Etiologic Factors including genetic, immunologic, infectious, and other factors relating to the cause of diabetes	5,566,665
3. Nutrition, Exercise, and Obesity	8,454,359
4. Hormones	19,330,805
5. Intermediary Carbohydrate and Protein Metabolism	11,934,133
6. Transplantation and Artificial Devices	4,688,831
7. Nonhormonal Blood Factors, Platelets, and Coagulation	1,582,179
8. Lipid Metabolism, Lipoproteins, Cholesterol, and Triglycerides	10,624,521
9. Pancreas and Islet Cell Studies	370,081
10. Microangiopathy	2,278,834
11. Macroangiopathy	1,324,148
12. Heart and Circulation	3,862,747
13. Central and Peripheral Nervous System	3,346,661
14. Nephropathy	1,635,040
15. Ocular Complications	15,482,911
16. Dental Complications	658,252
17. Infections	1,178,171
18. Pregnancy and Perinatal Problems	4,254,662
19. Psychosocial and Behavioral Problems	1,346,194
20. Pharmacologic Agents	1,910,733
21. Epidemiology	3,405,269
22. Health Services	3,000*
Subtotal · Research	**$105,607,647**
C. Health Care Delivery	
1. Health Care Facilities and Research	439,529
2. Health Care Services	1,157,928
3. Social Adjustment and Mental Health Services	439,529
4. Public Education	440,529
5. Patient Education	440,529
6. Quality Assurance	440,529
7. Health Care Financing	440,529
8. Health Planning and Evaluation	
Subtotal · Health Care Delivery	$ 3,358,573
D. Manpower Development and Professional Education	
1. General	2,492,325
2. Career Awards	4,508,028
3. Fellowships and Training Programs	
Subtotal · Manpower Development and Professional Education	$ 7,000,353
E. Multidisciplinary Programs	$ 12,020,997
F. Workshops, Conferences, and Publications	$ 175,125
G. Unclassified	$ 298,124
TOTAL**	**$128,460,819**

* *Funding amounts for CDC, NCHS, and VA were not provided for inclusion.*

** *Includes some diabetes-related intramural funds.*

Table 2.—FY 1979 diabetes-related funding by subject area and agency ($ thousands)[a]

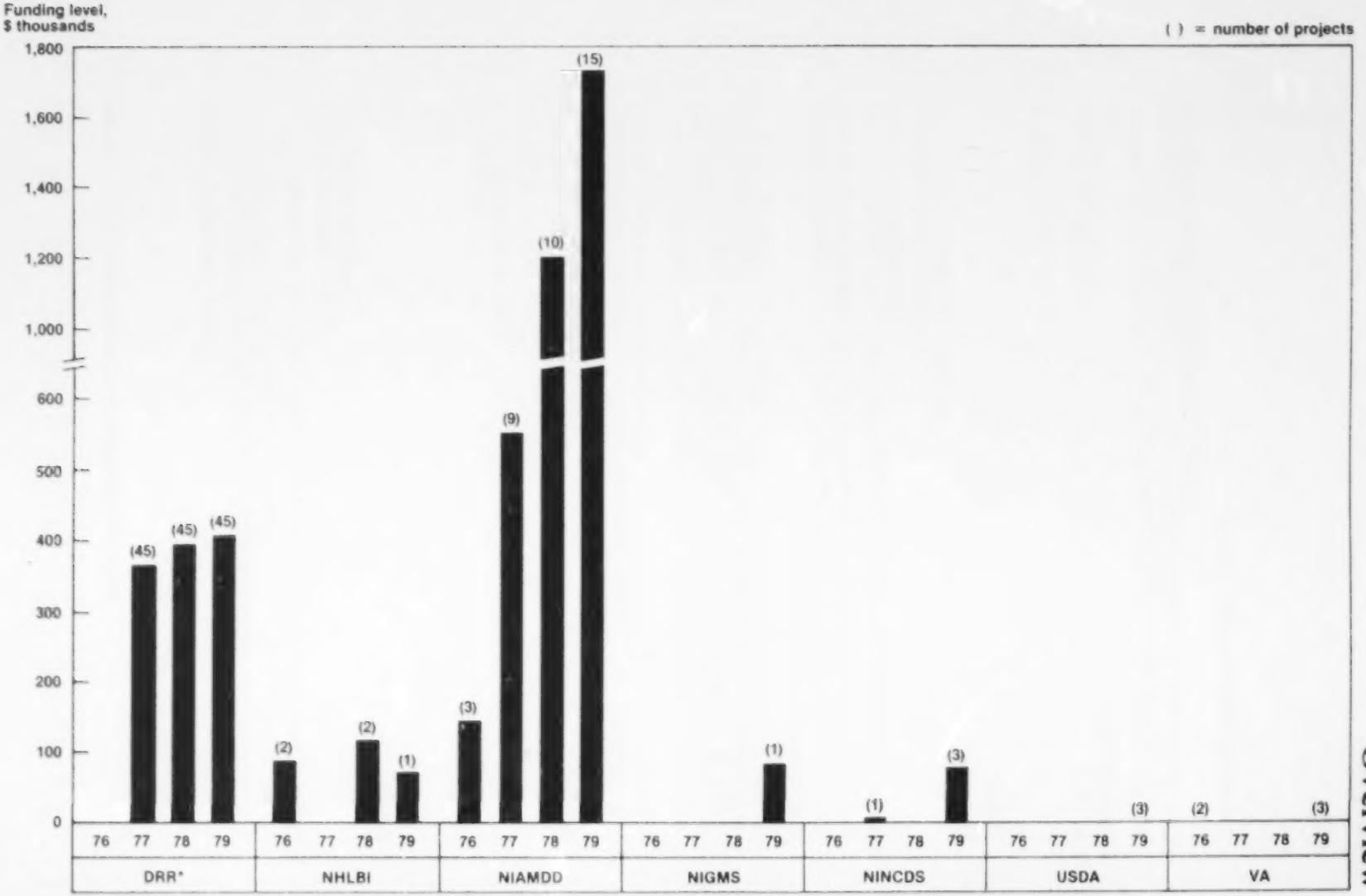
	ADAMHA	CDC[b]	DRR	FDA	HRA	NCHS	NEI	NHLBI	NIA	NIAID	NIAMDD	NICHD	NIDR	NIEHS	NIGMS	NINCDS	USDA	VA
A. Epidemiology (see B.21)																		
B. Research																		
1. Resources			403					72			1,734				61	79	X	X
2. Etiologic Factors including genetic, immunologic, infectious, and other factors relating to the cause of diabetes			369				270	14		1,293	2,631	368	420	100	101		X	X
3. Nutrition, Exercise, and Obesity			2,281						159		3,873	1,190	90			201	980	X
4. Hormones	274		1,781	18				440	852	215	15,590	78			82		X	X
5. Intermediary Carbohydrate and Protein Metabolism			274						109		8,809	815			509	1,219	199	X
6. Transplantation and Artificial Devices			114					83		18	4,262	43			168			X
7. Nonhormonal Blood Factors, Platelets, and Coagulation			40					1,191			351							
8. Lipid Metabolism, Lipoproteins, Cholesterol, and Triglycerides			417					3,776	158		6,043	53			184	13		X
9. Pancreas and Islet Cell Studies									50	22	298							
10. Microangiopathy			65				104	1,375			582		110			42		X
11. Macroangiopathy			16					909	140							259		X
12. Heart and Circulation			64					3,671			101				26			X
13. Central and Peripheral Nervous System			111					172			902		70			2,091		X
14. Nephropathy			126					121		126	1,262							X
15. Ocular Complications			18				15,235	229										X
16. Dental Complications			13										645					X
17. Infections			72							1,009	97							X
18. Pregnancy and Perinatal Problems			605					385			632	2,632					X	
19. Psychosocial and Behavioral Problems	190		196					411			549							X
20. Pharmacologic Agents	X		1,008					21			794				87			X
21. Epidemiology		X				X	468	1,324			1,538				75		X	X
22. Health Services		X	3			X												X
Subtotal	**464**		**7,976**	**18**			**16,077**	**14,194**	**1,468**	**2,683**	**50,048**	**5,179**	**1,335**	**100**	**1,293**	**3,904**	**859**	
C. Health Care Delivery																		
1. Health Care Facilities and Research																		
2. Health Care Services		440				X												
3. Social Adjustment and Mental Health Services																		
4. Public Education		441	378															
5. Patient Education		440									339							
6. Quality Assurance		441																
7. Health Care Financing		441				X												
8. Health Planning and Evaluation		441																
Subtotal		**2,644**	**378**								**339**							
D. Manpower Development and Professional Education																		
1. General																		
2. Career Awards							157	241		41	2,053							
3. Fellowship and Training Programs	36				354		74	67		12	3,952	13						
Subtotal	**36**				**354**		**231**	**308**		**53**	**6,005**	**13**						
E. Multidisciplinary Programs											**9,143**	**2,615**				**264**		
F. Workshops, Conferences, and Publications											175							
G. Unclassified											**200**				**94**			
TOTAL FY 1979 FUNDING[c]	**500**	**2,644**	**8,354**	**18**	**354**	**X**	**16,308**	**14,502**	**1,468**	**2,736**	**65,910**	**7,807**	**1,335**	**100**	**1,387**	**4,168**	**859**	**X**

X Entries are inexact due to rounding of individual project amounts. X indicates activity reported but no funding data provided.

[b] CDC diabetes control demonstration projects cross-cut reporting categories B.21.22, C.2, and C.4.4.

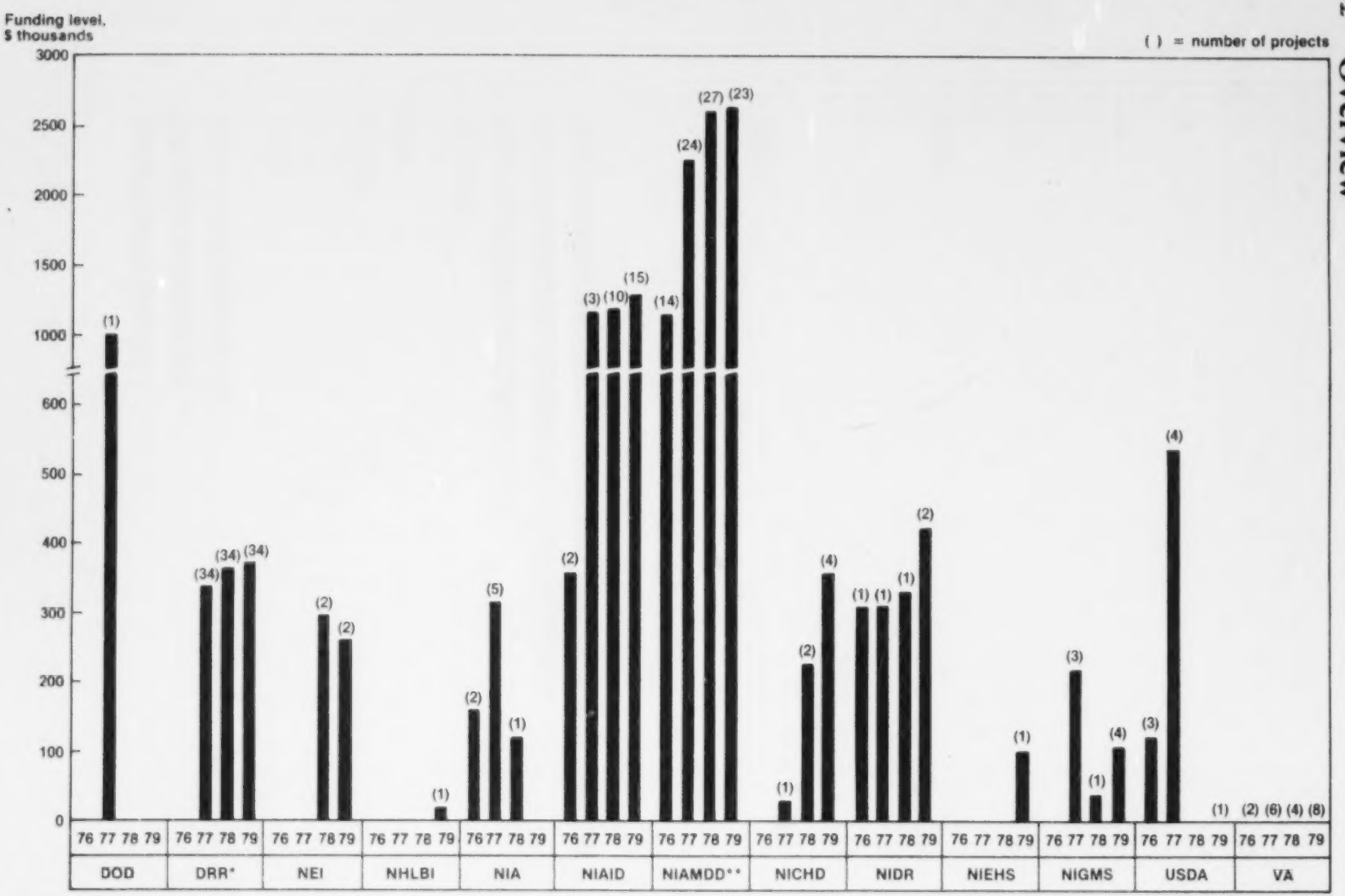
[c] May include some diabetes-related intramural funds.

Resources (B 1)



*DRR provided data for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

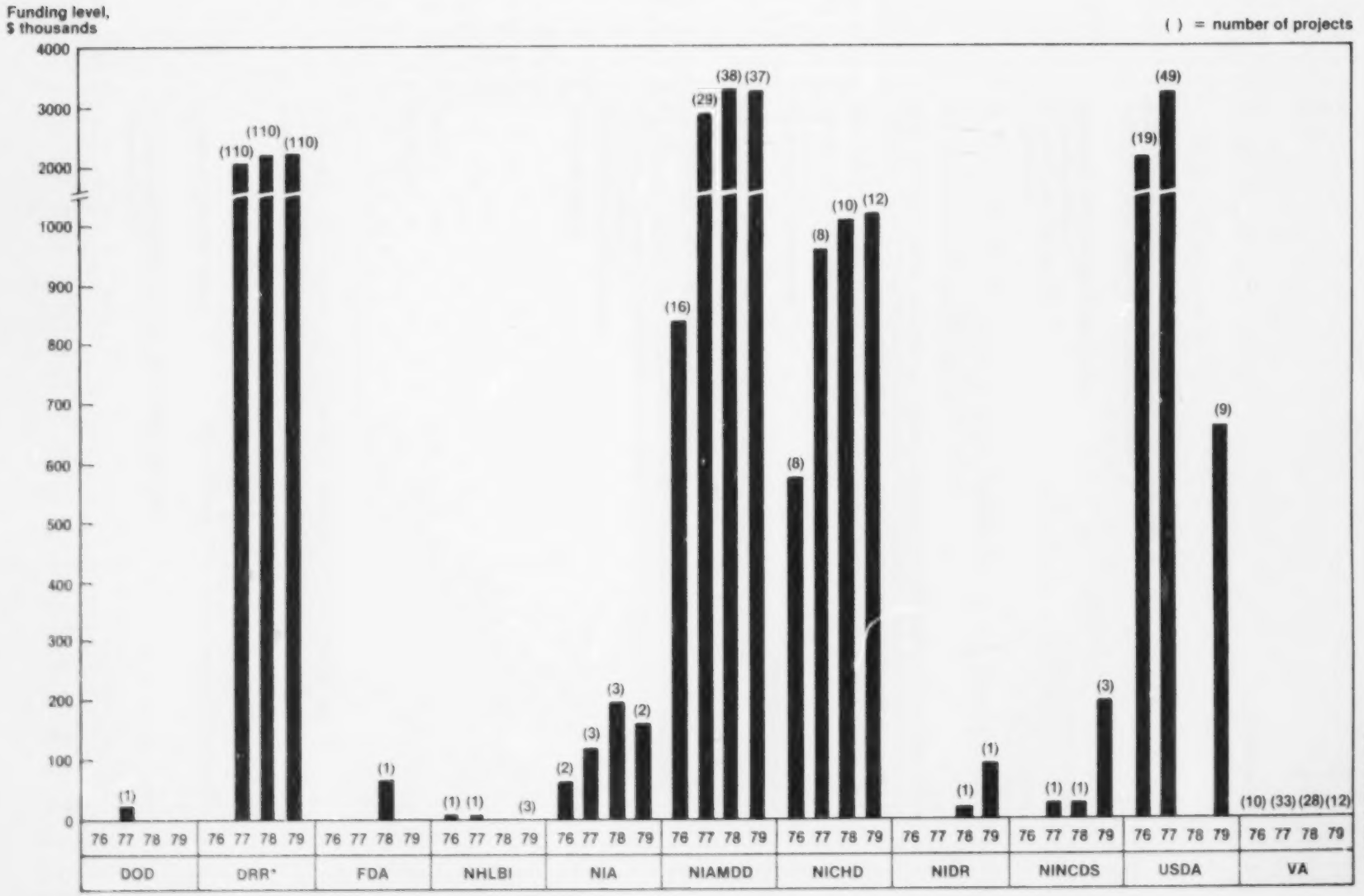
Etiologic Factors (B 2)



*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

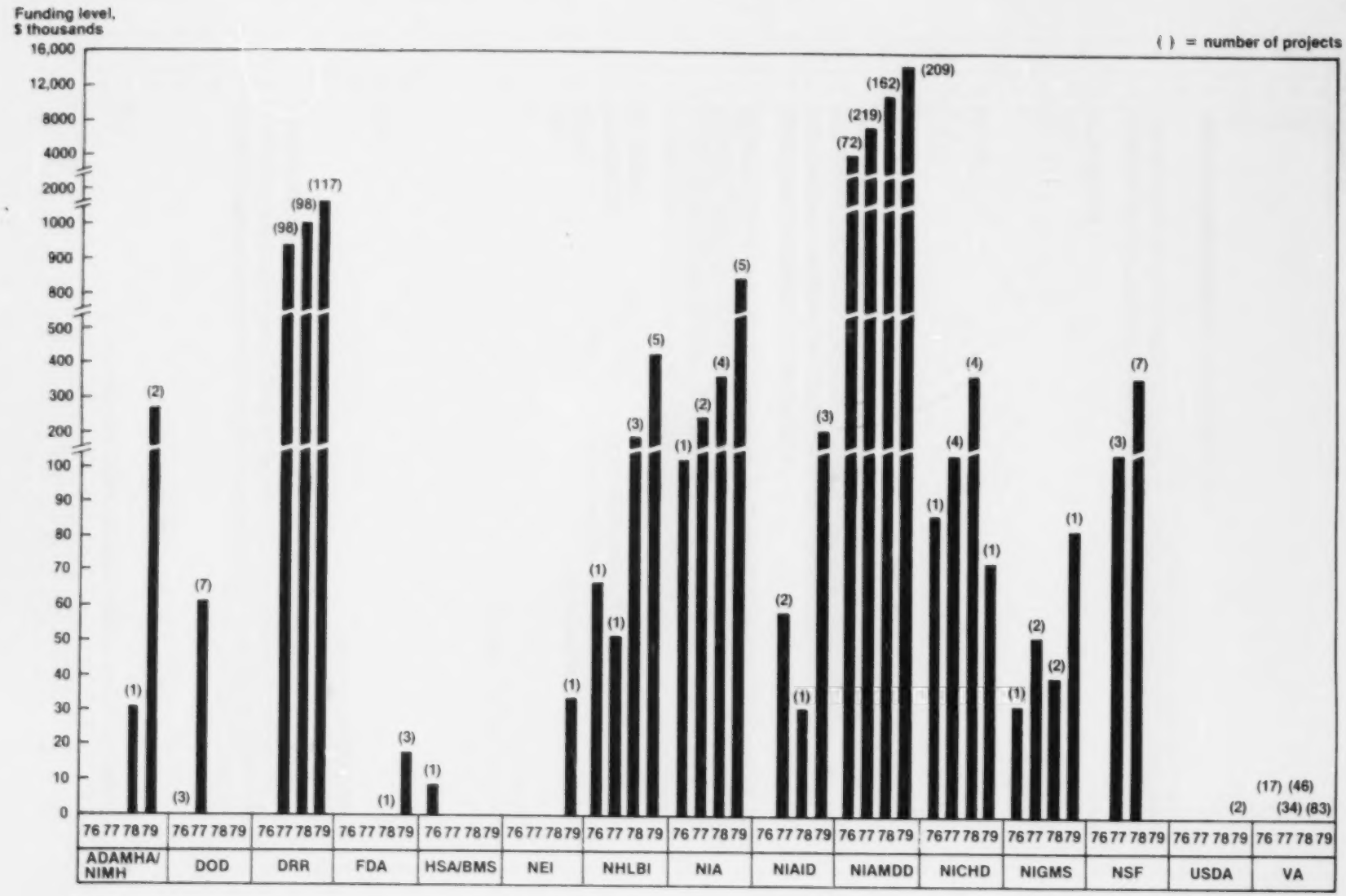
**FY 1976 figures have been adjusted from those included in the third annual report to correct duplicate reporting of HSA/IHS activities funded and also reported by NIAMDD.

Nutrition, Exercise, and Obesity (B 3)

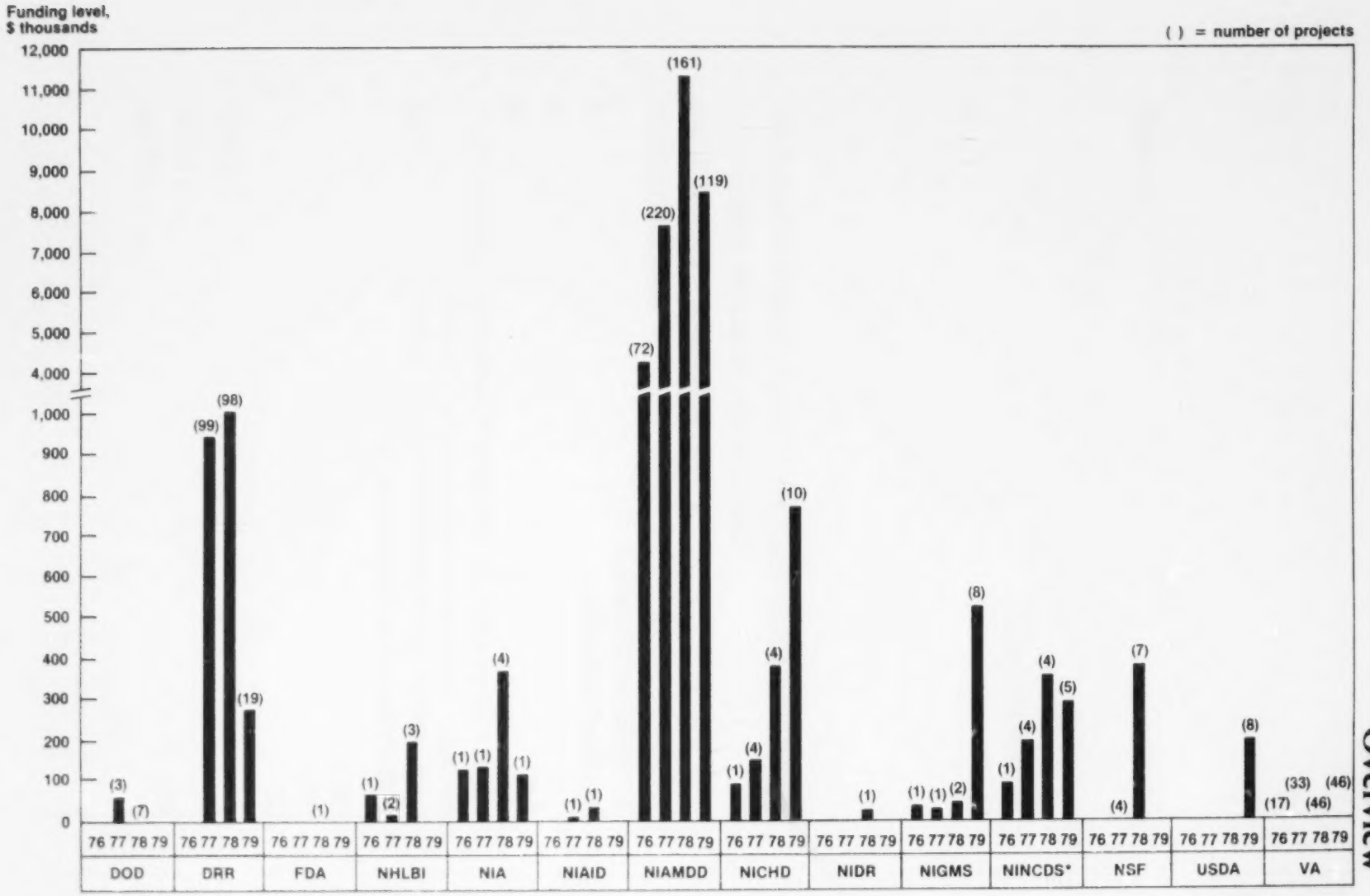


*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

Hormones (B 4)

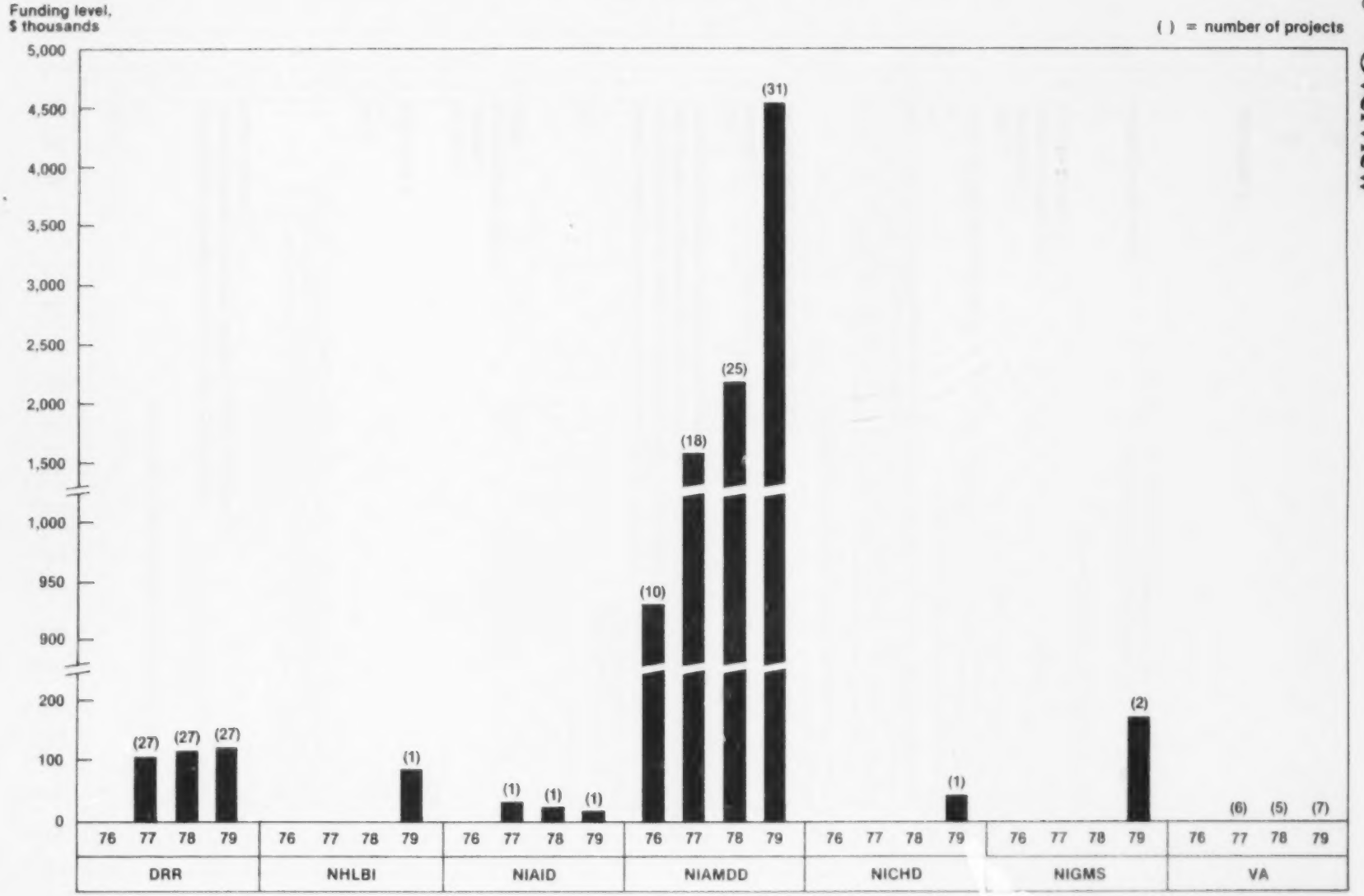

Funding level, $ thousands
( ) = number of projects
16,000
12,000
8000
4000
2000
1000
900
800
500
400
300
200
100
90
80
70
60
50
40
30
20
10
0
(1)
(2)
(3)
(7)
(98)
(98)
(117)
(1)
(3)
(1)
(1)
(1)
(3)
(1)
(5)
(1)
(2)
(4)
(5)
(2)
(1)
(3)
(72)
(219)
(162)
(209)
(1)
(4)
(4)
(1)
(1)
(2)
(2)
(1)
(3)
(7)
(2)
(17) (46)
(34) (83)
76 77 78 79
ADAMHA/ NIMH
DOD
DRR
FDA
HSA/BMS
NEI
NHLBI
NIA
NIAID
NIAMDD
NICHD
NIGMS
NSF
USDA
VA

Intermediary Carbohydrate and Protein Metabolism (B 5)

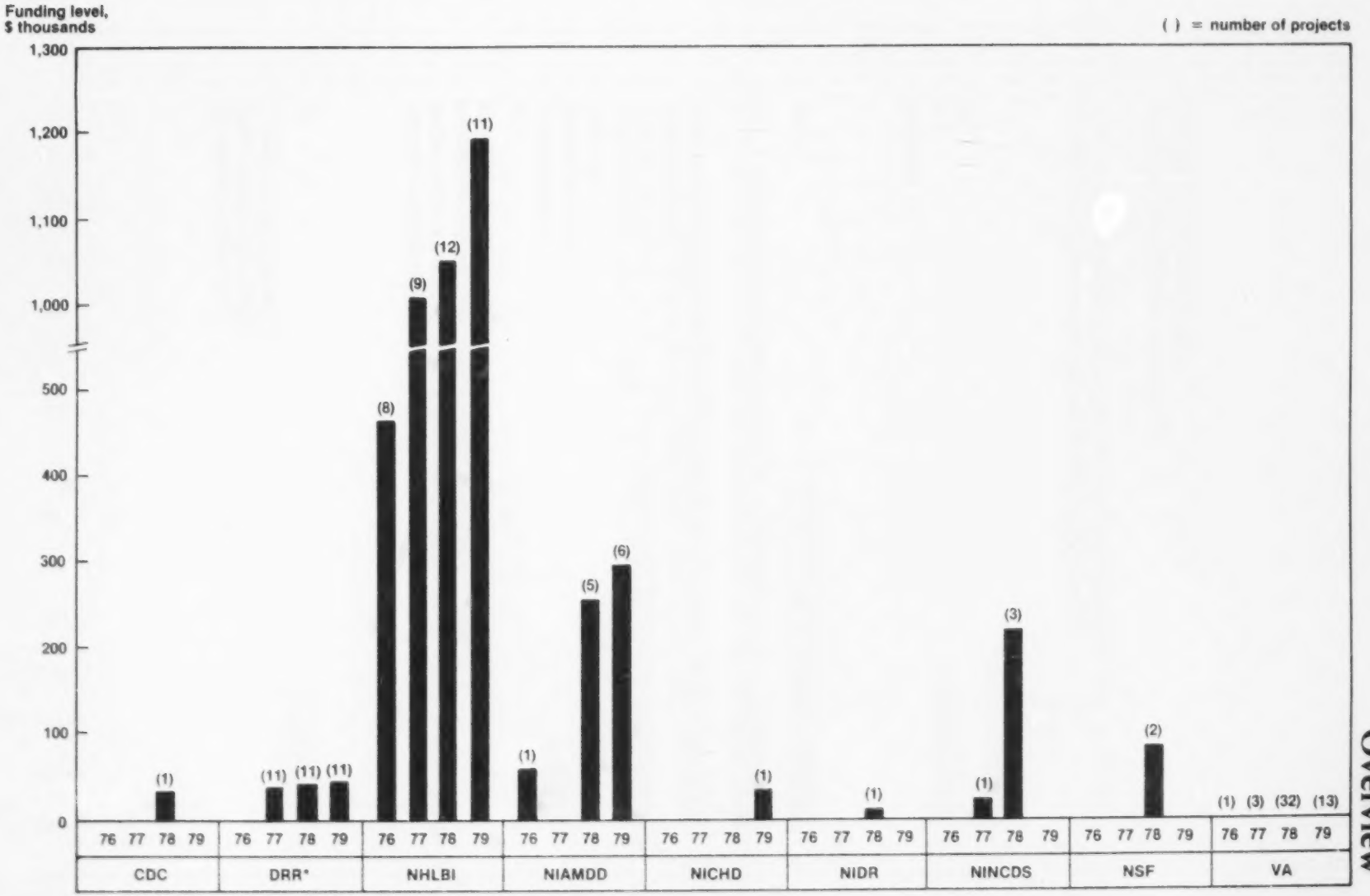


*Funding data for three FY 1979 projects were not available for inclusion.

Transplantation and Artificial Devices (B 6)

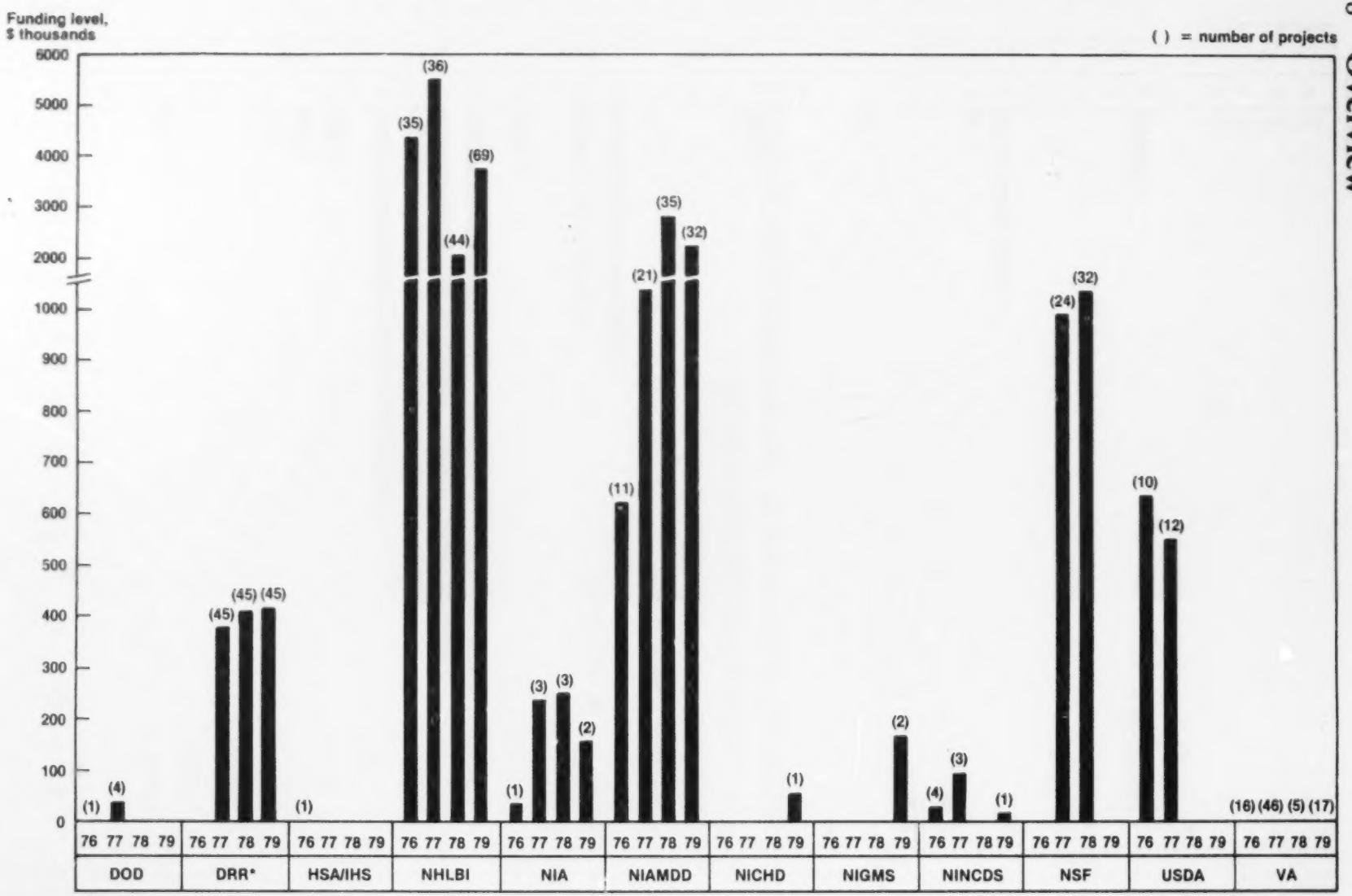


Nonhormonal Blood Factors, Platelets, and Coagulation (B 7)



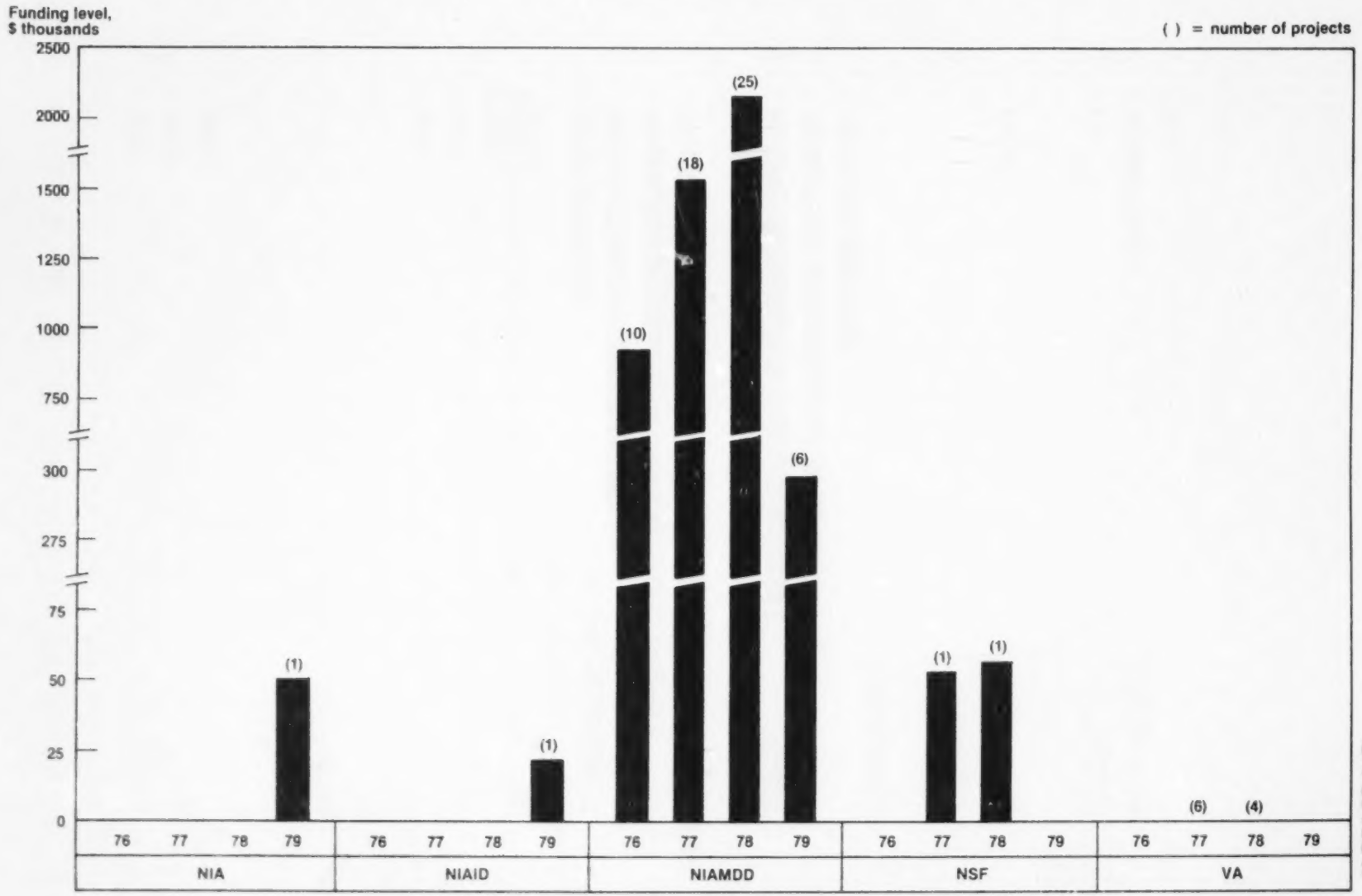
*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

Lipid Metabolism, Lipoproteins, Cholesterol, and Triglycerides (B 8)

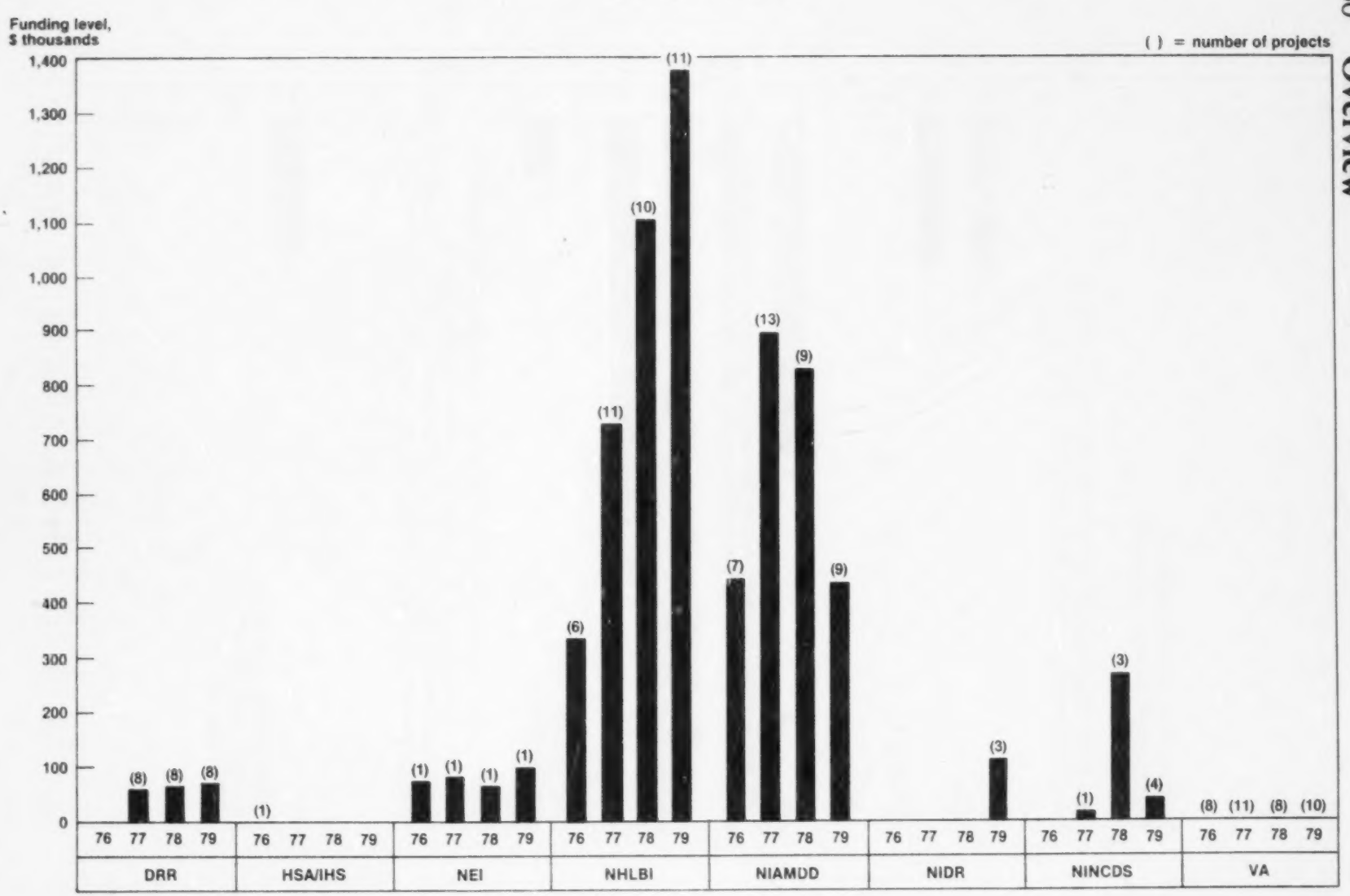


*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

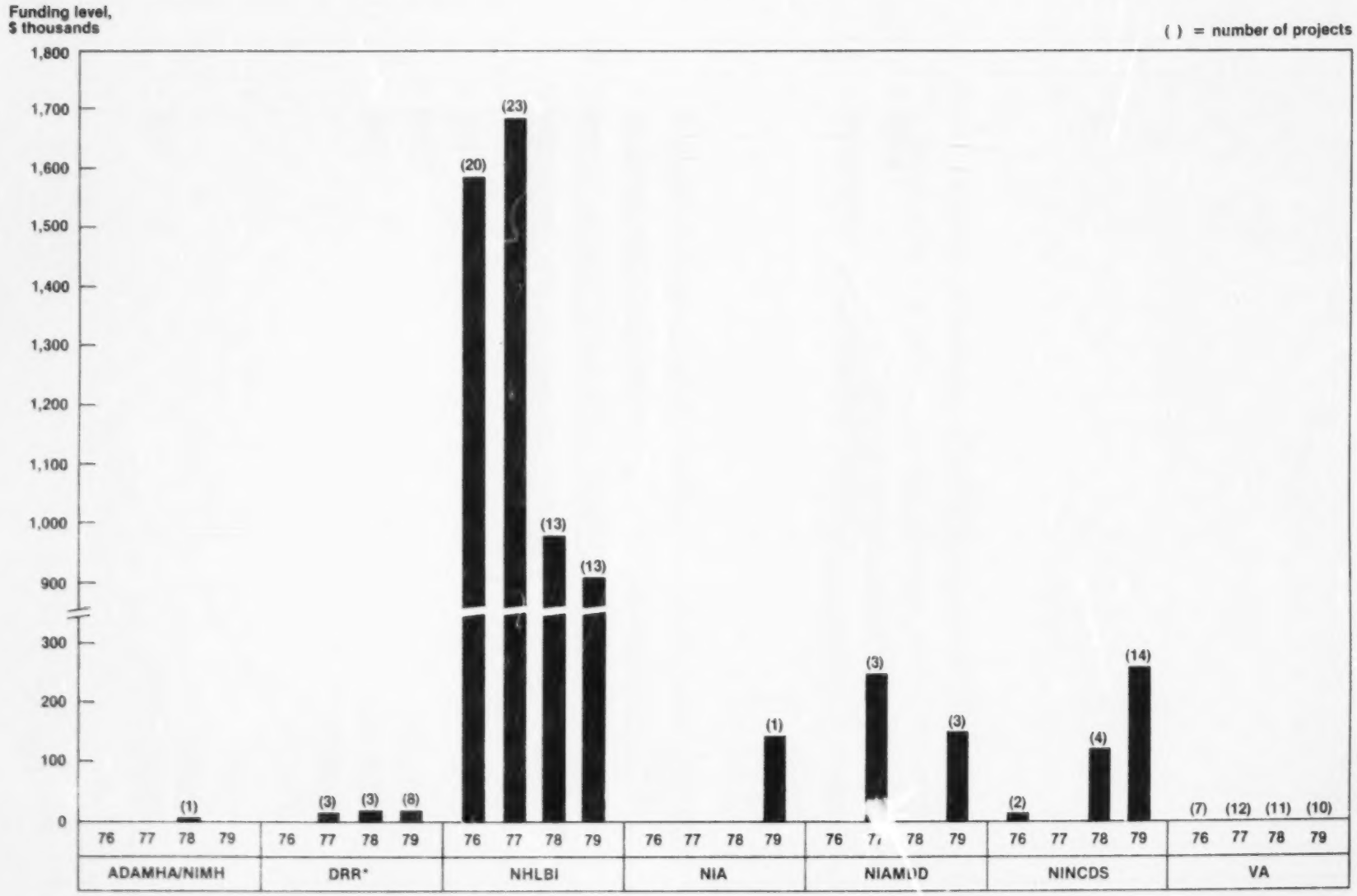
Pancreas and Islet Cell Studies (B 9)



Microangiopathy (B 10)

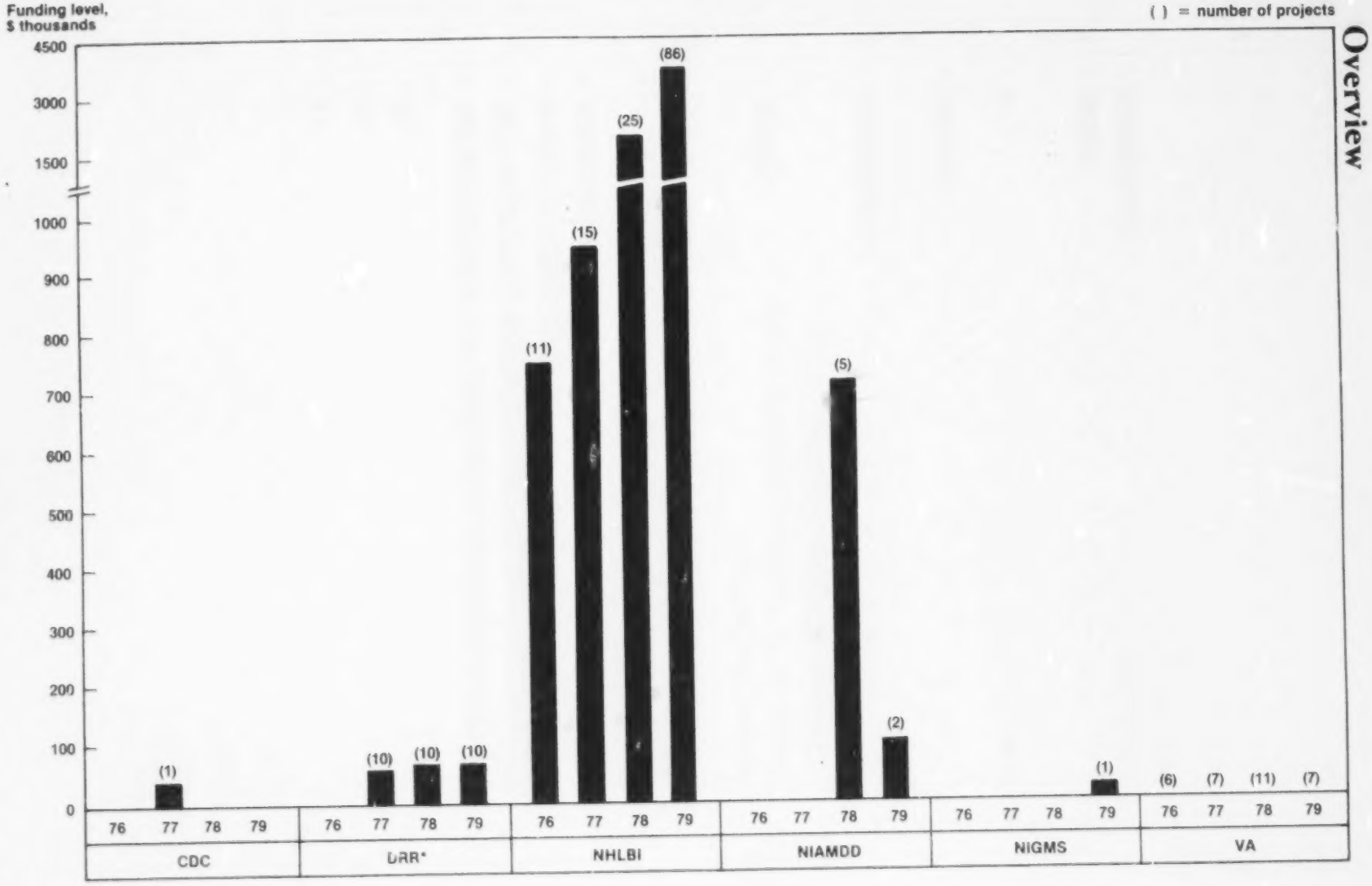


Macroangiopathy (B 11)



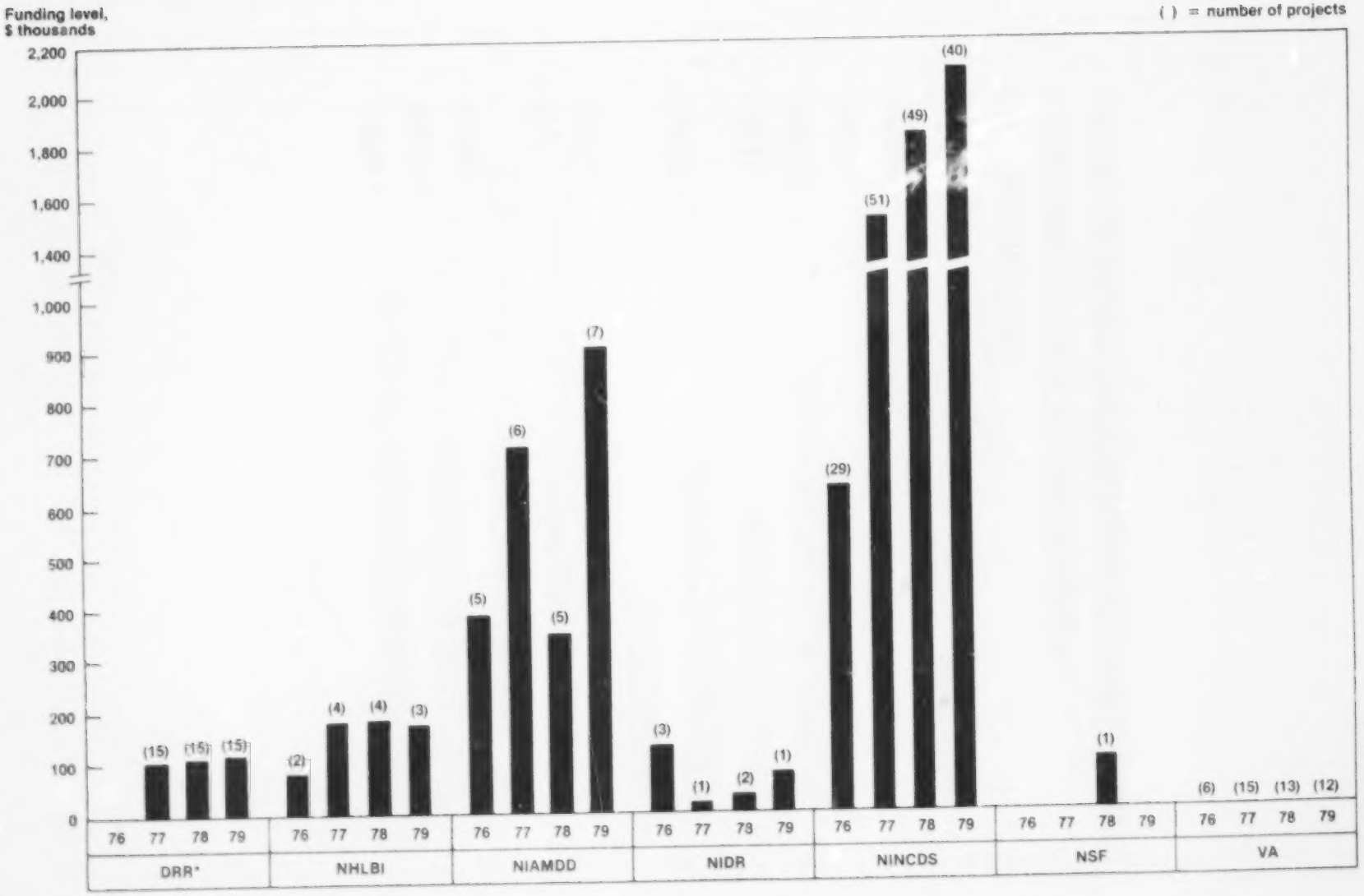
*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

Heart and Circulation (B 12)



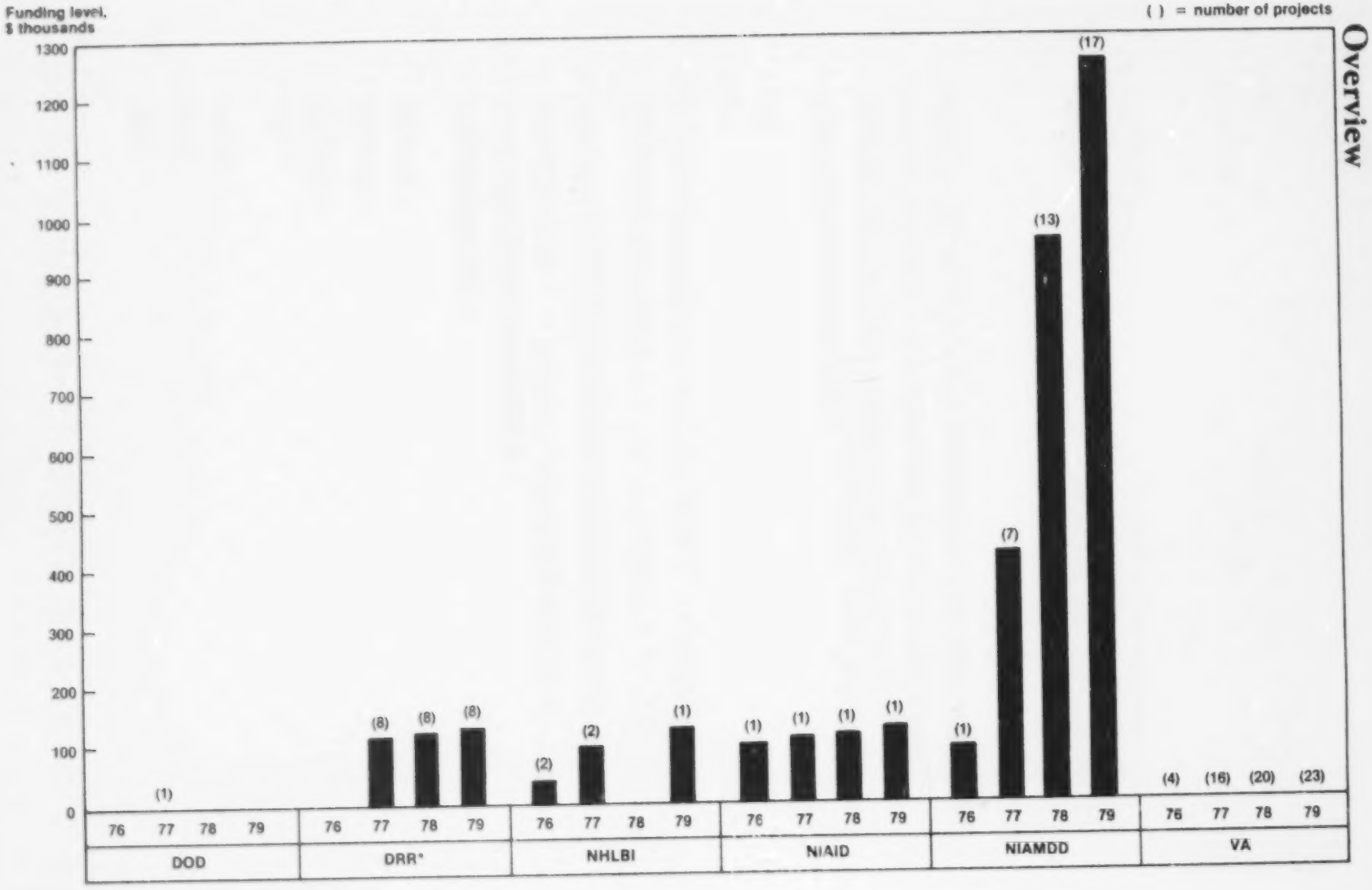
*DRR data reported for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

Central and Peripheral Nervous System (B 13)



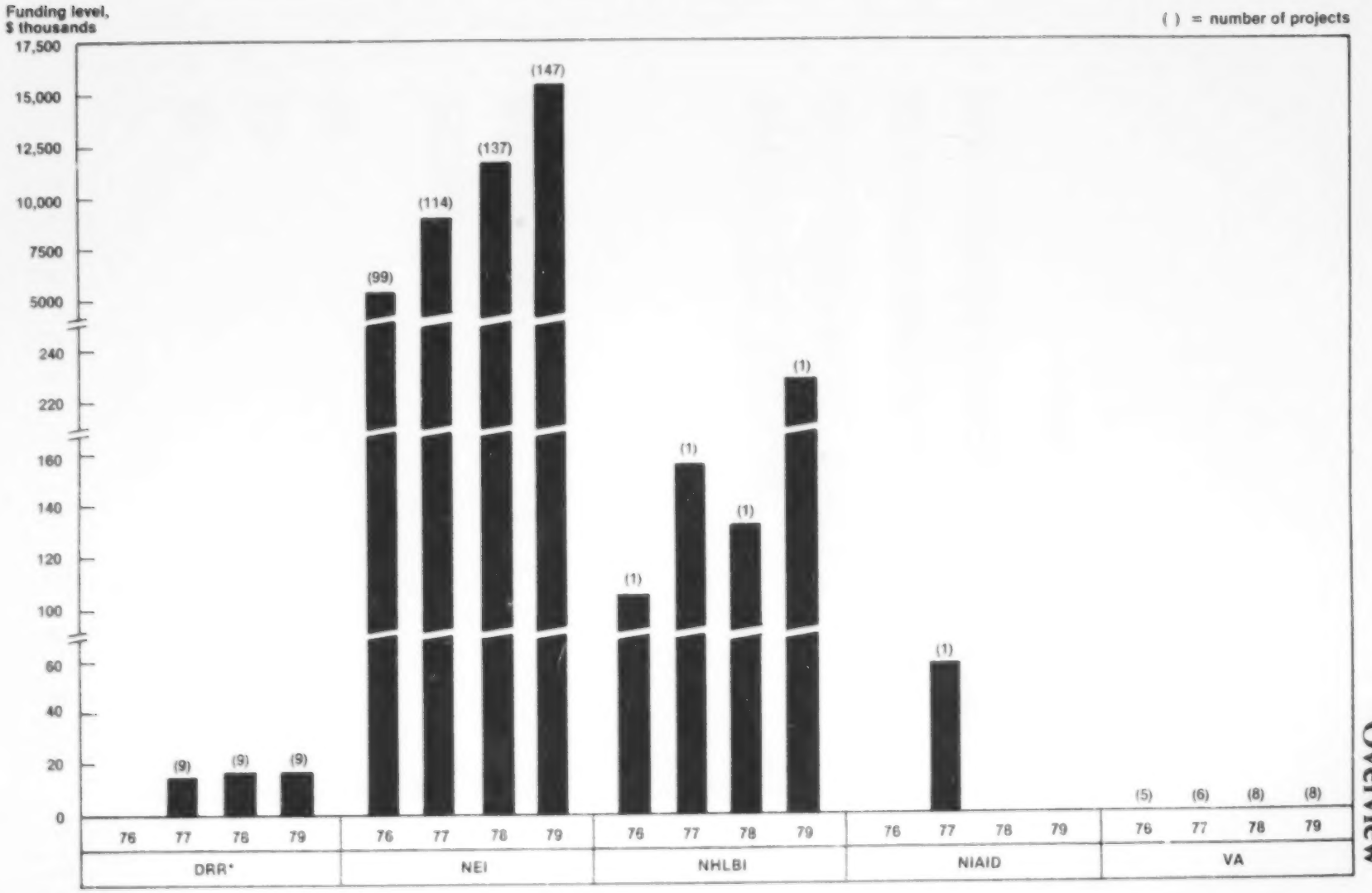
*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated only).

Nephropathy (B 14)



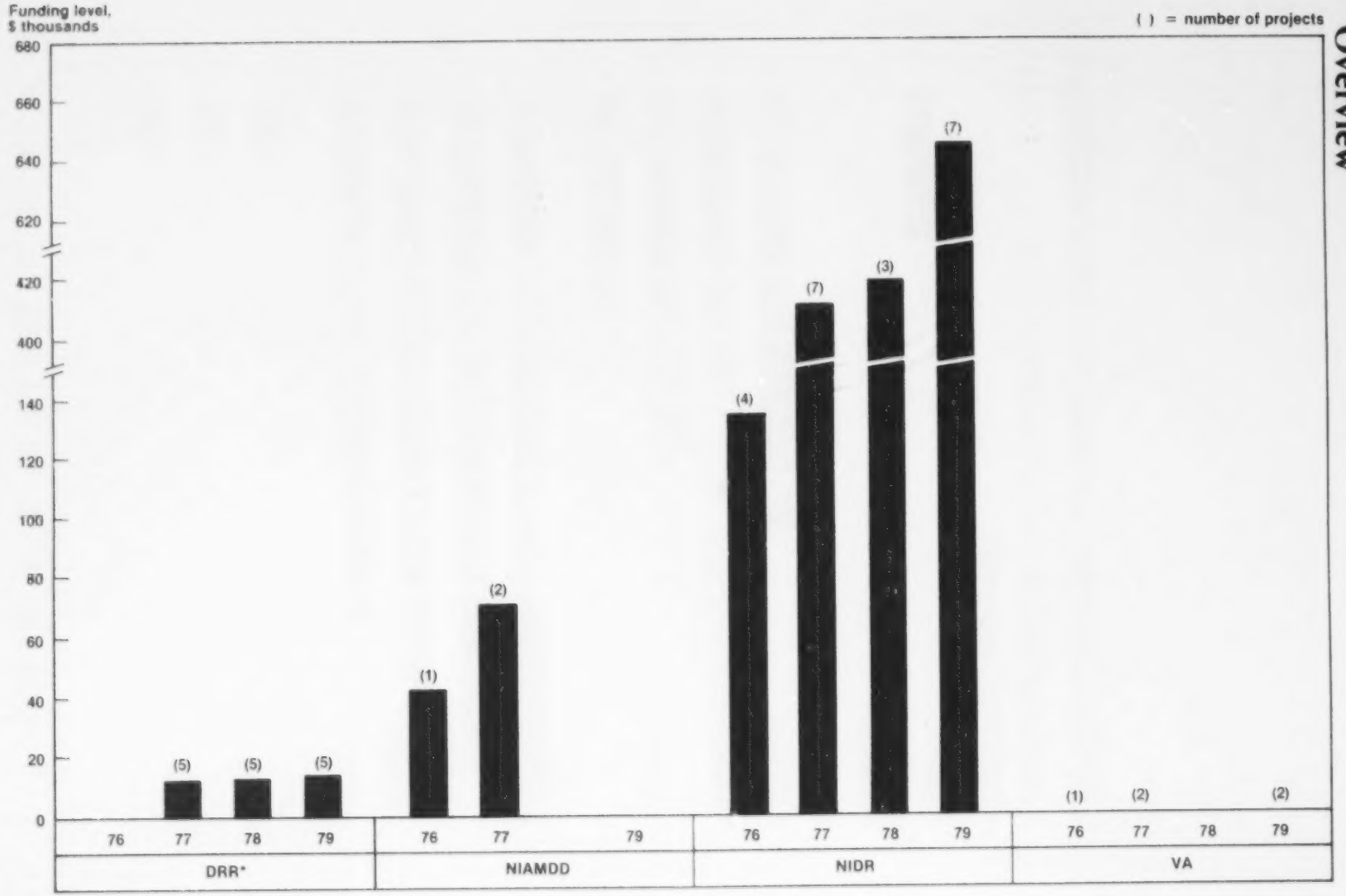
*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only

Ocular Complications (B 15)



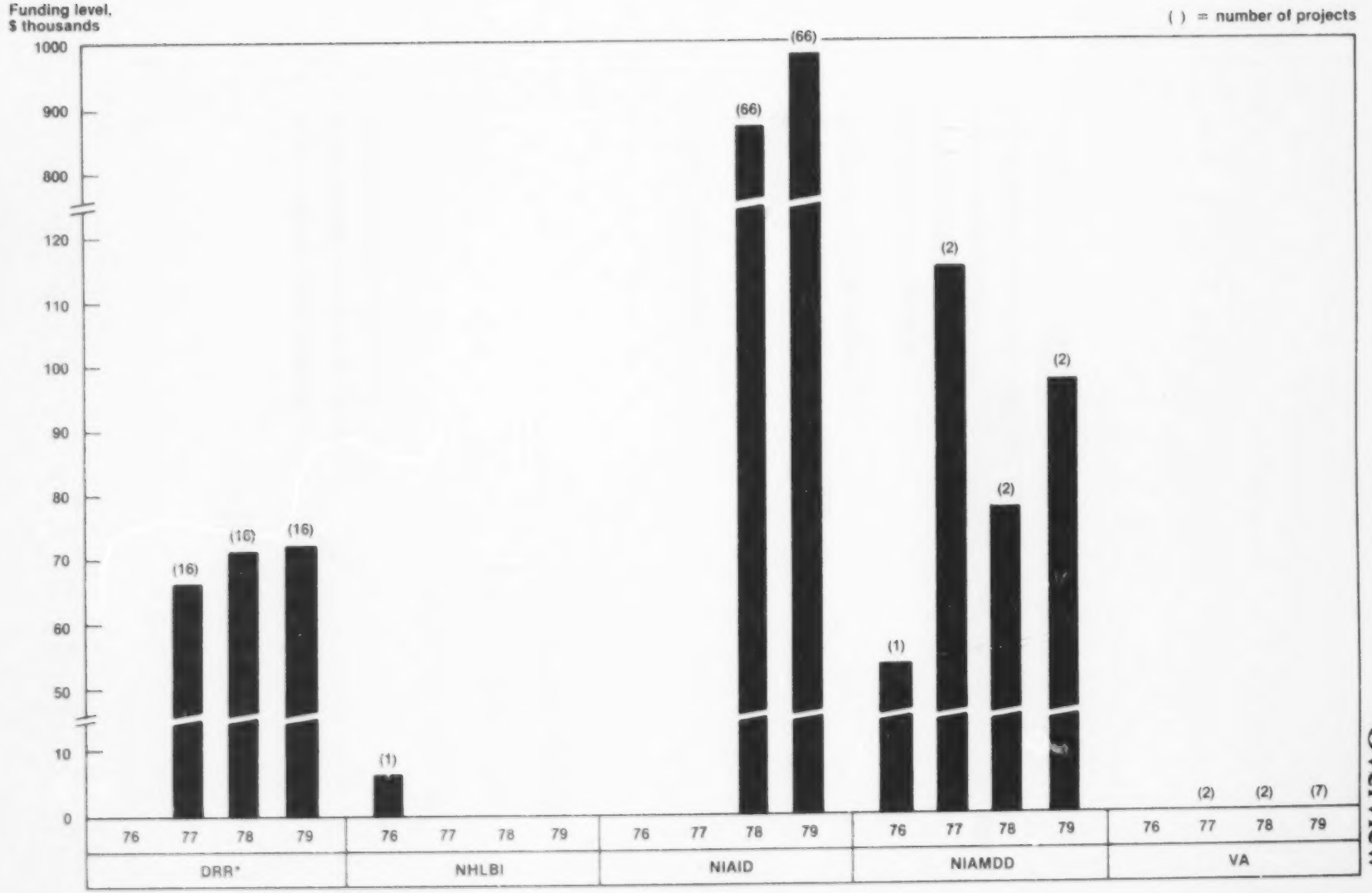
*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

Dental Complications (B 16)



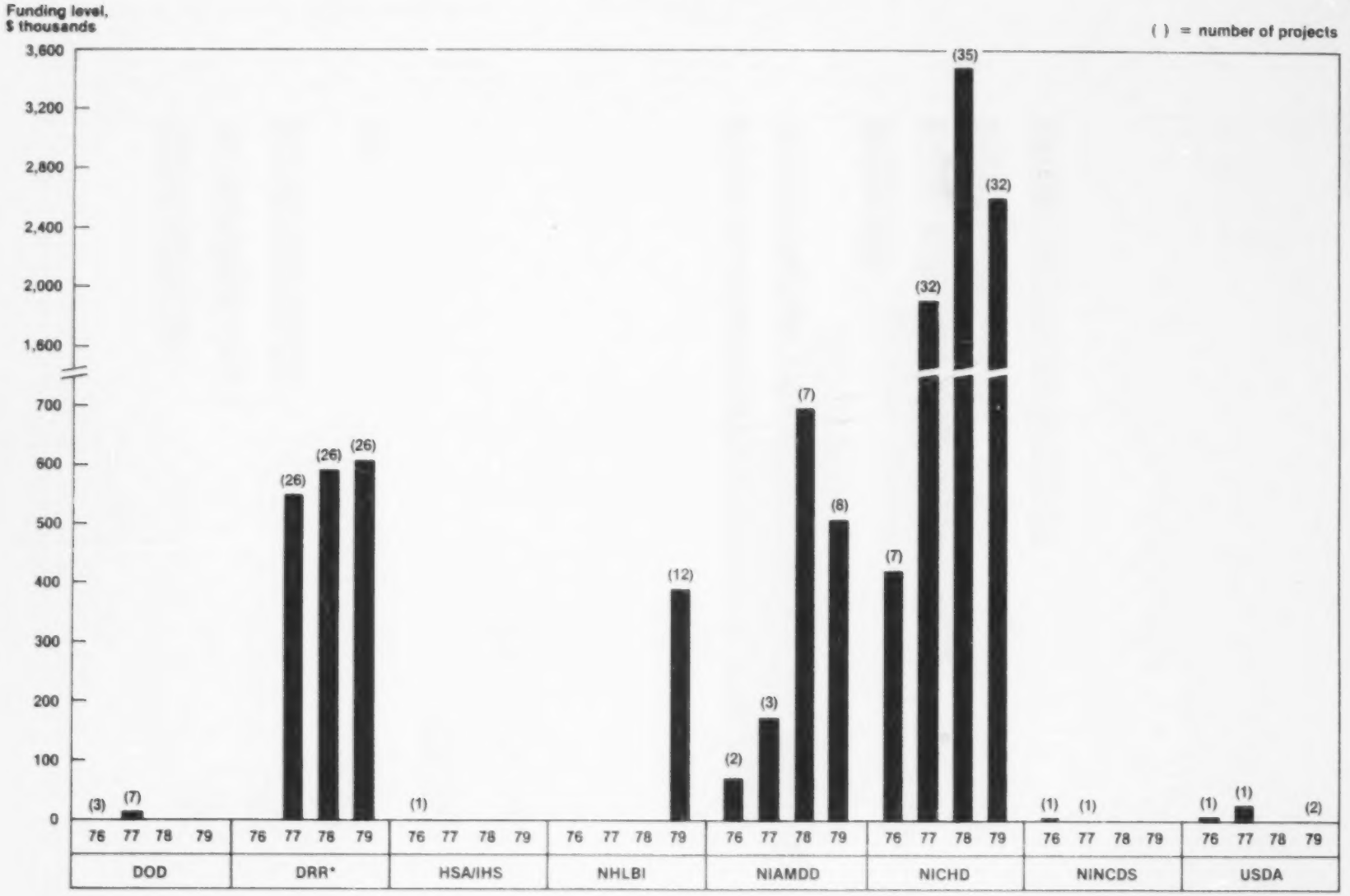
*DRR data provided for F.Y. 1977 (actual), F.Y. 1978 (estimated), and F.Y. 1979 (estimated) only.

Infections (B 17)



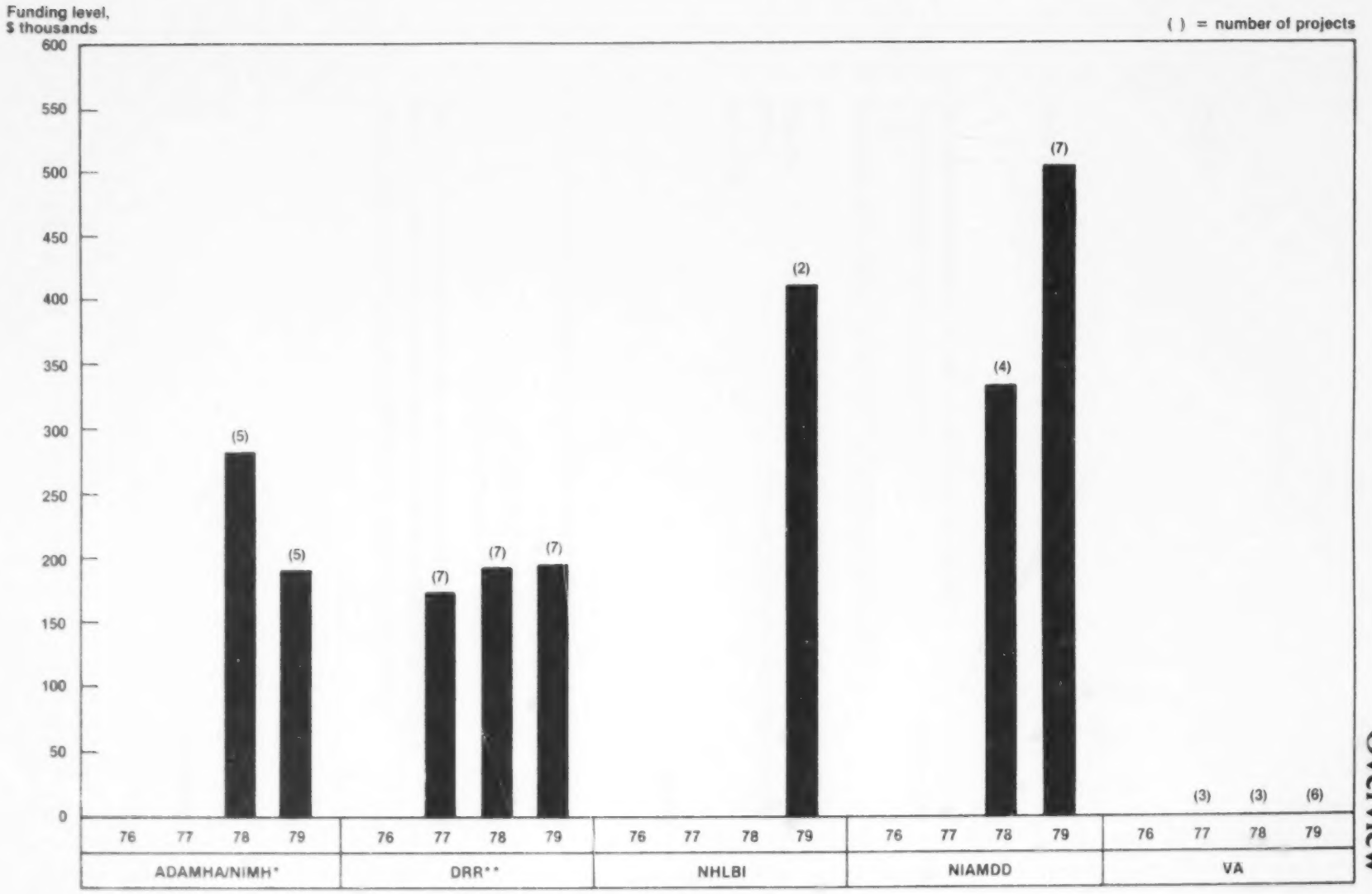
*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

Pregnancy and Perinatal Problems (B18)



*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

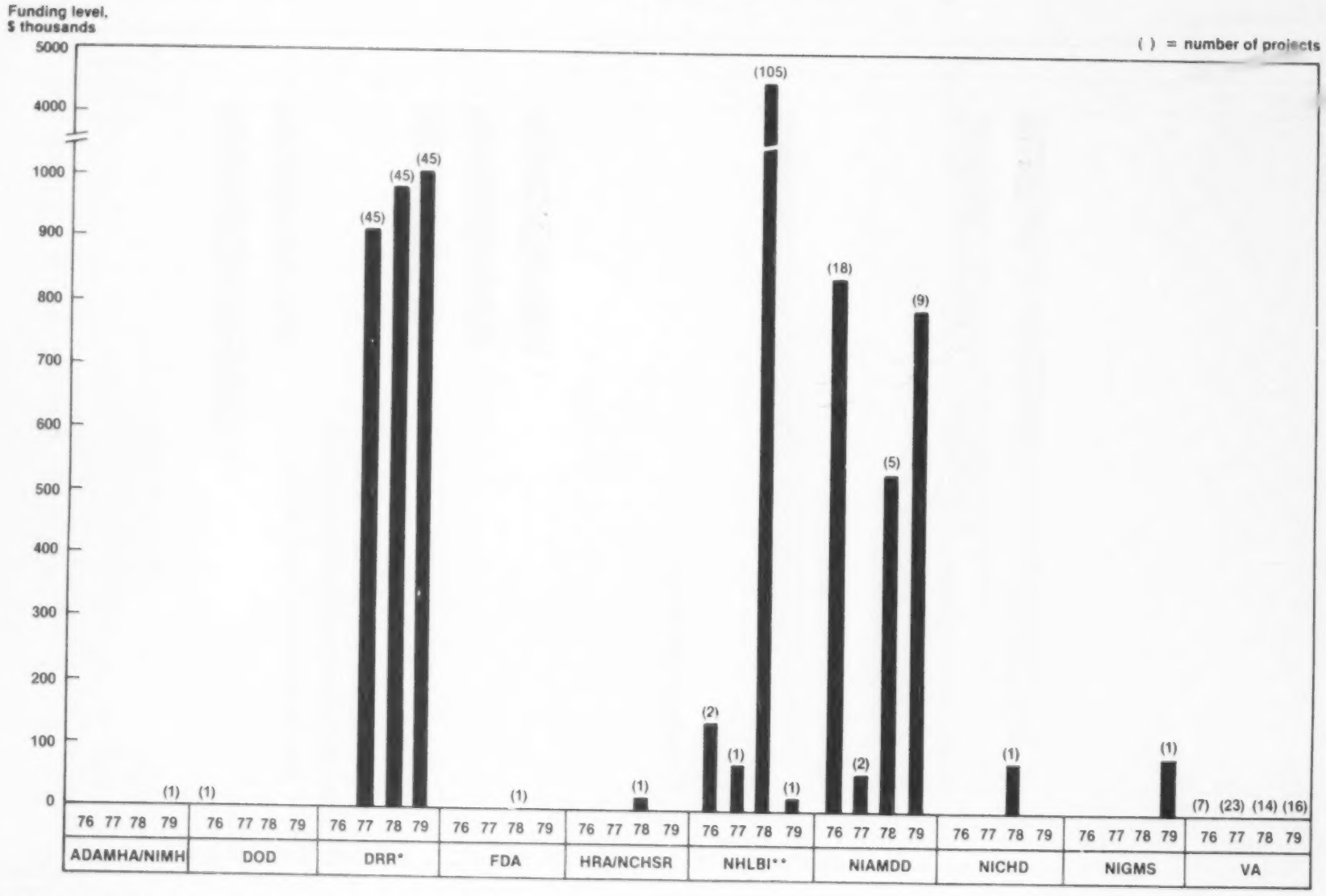
Psychosocial and Behavioral Problems (B 19)



*Funding data for two FY 1979 projects not available.

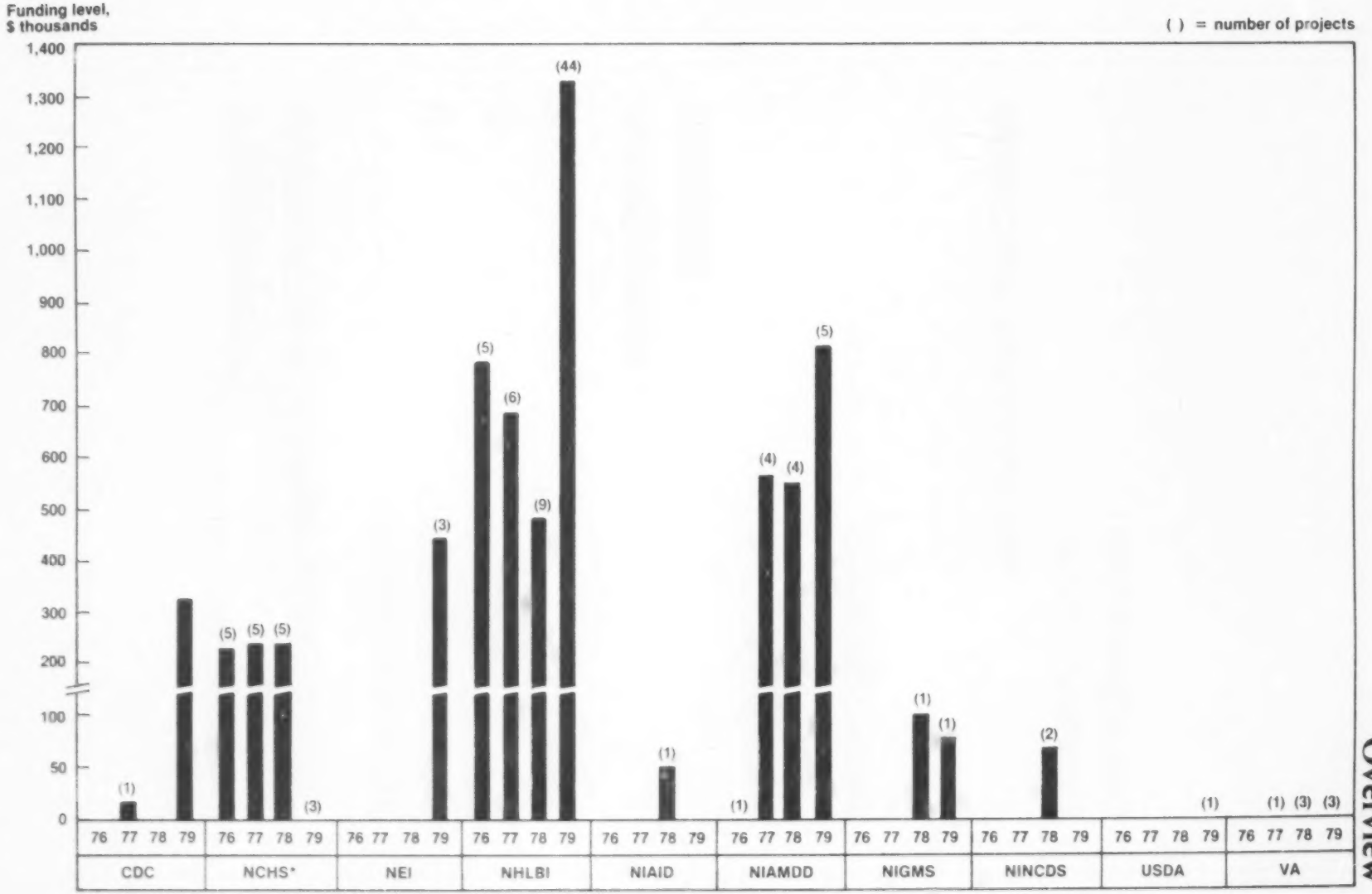
**DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

Pharmacologic Agents (B 20)



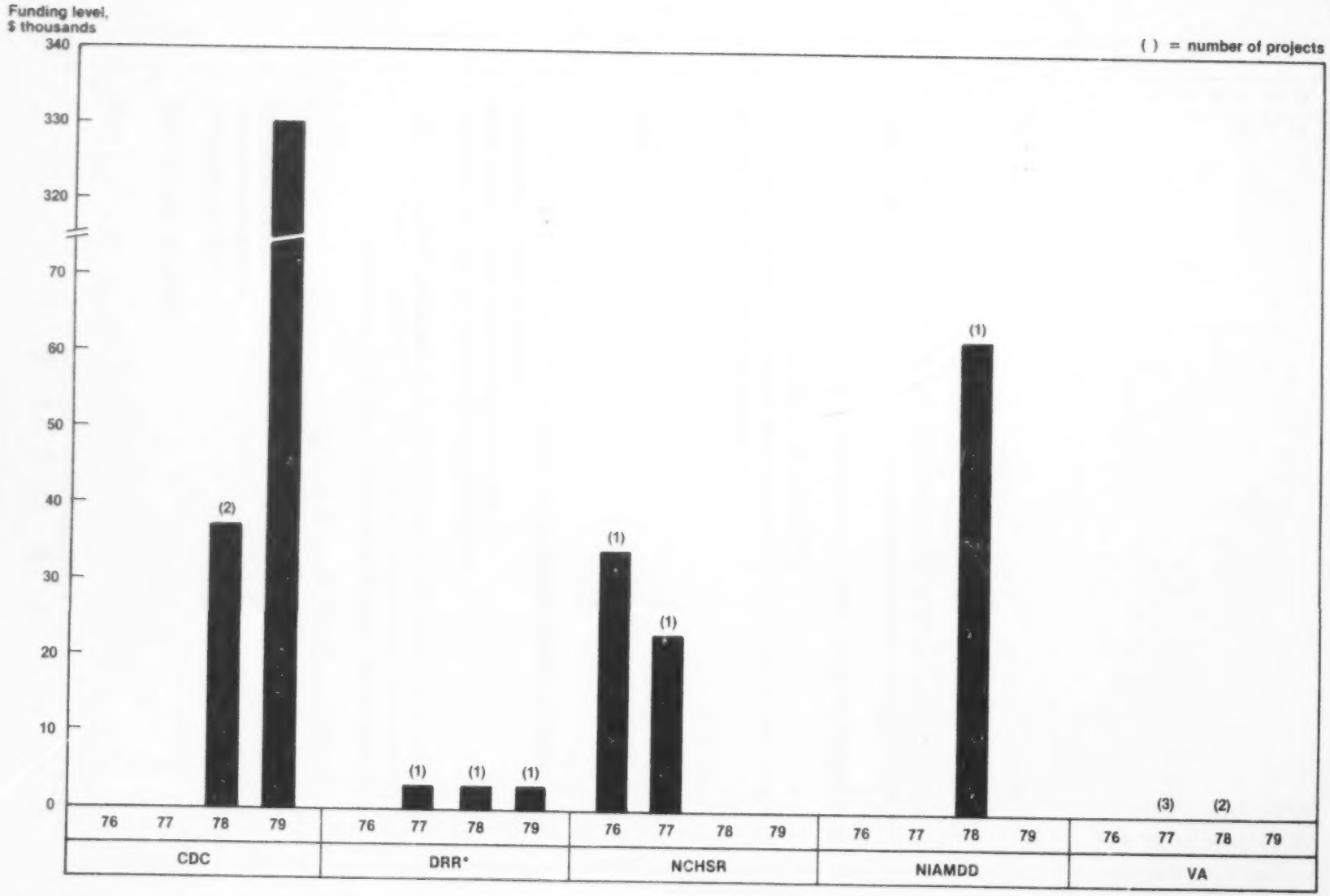
*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.
**NHLBI drops from 105 projects in FY 1978 to 1 in FY 1979 because of reclassification.

Epidemiology (B 21)



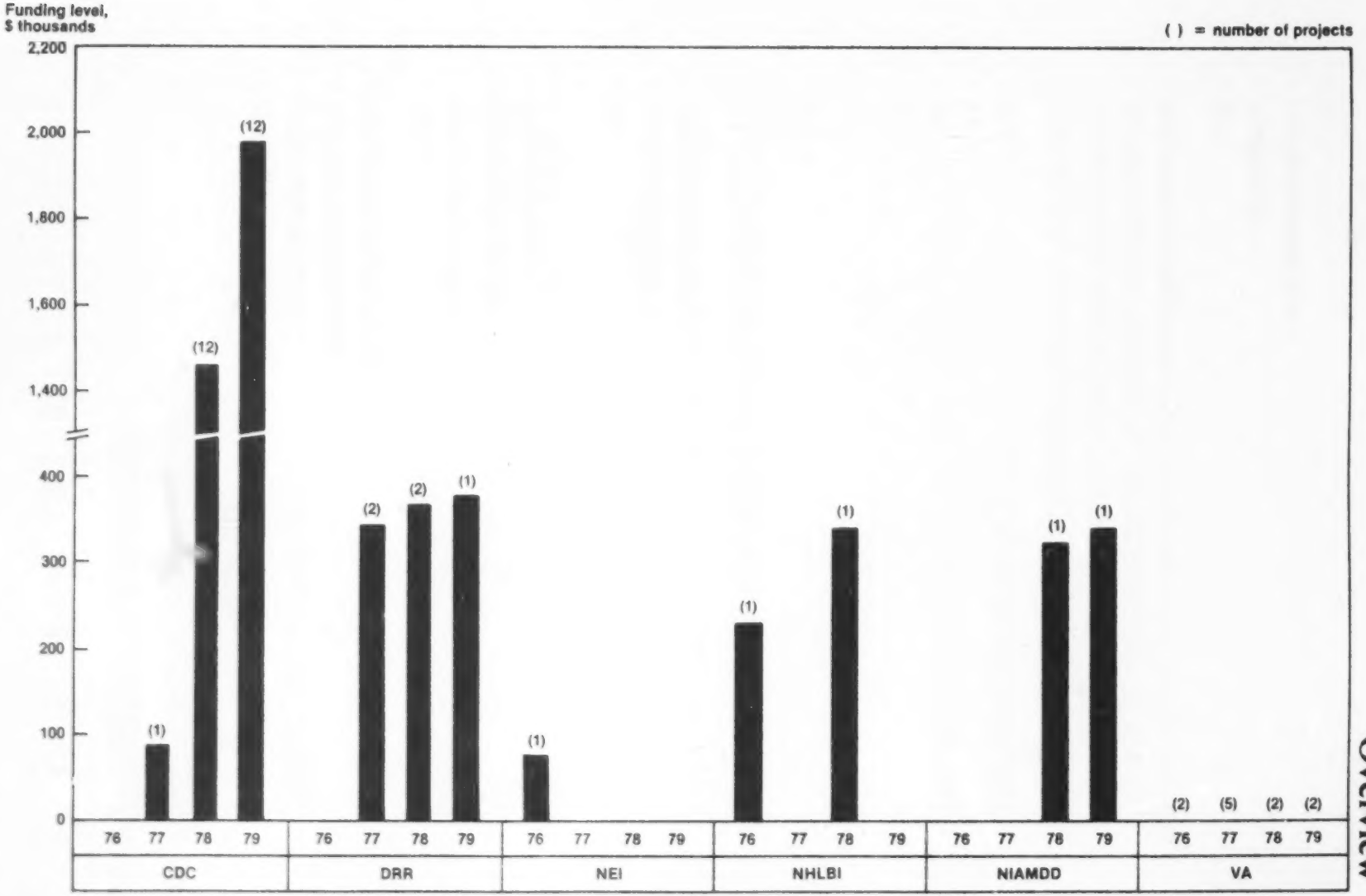
*FY 1977 values have been changed from those in fourth annual report to correct for previous nonreporting

Health Services (B 22)

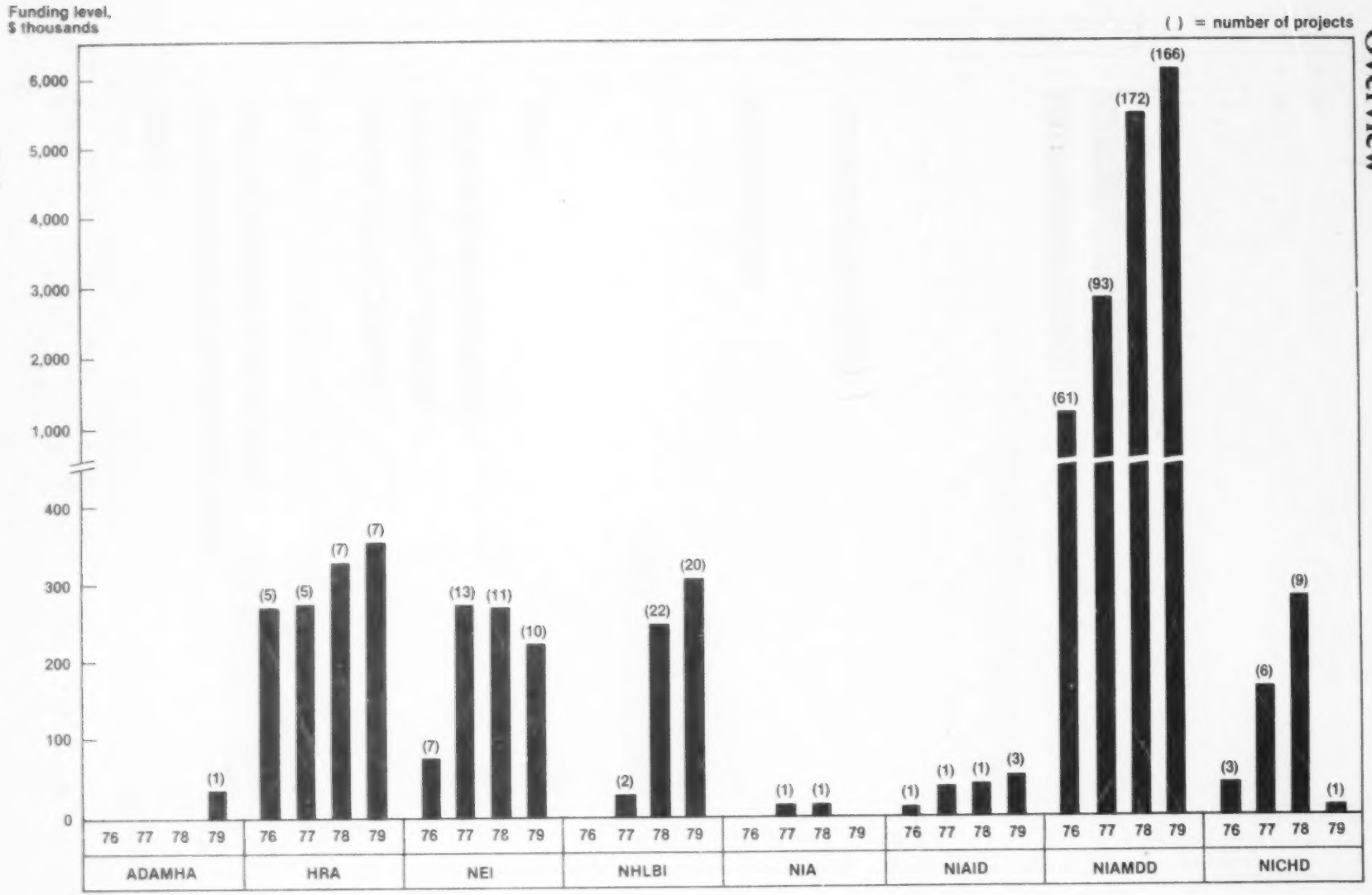


*DRR data provided for FY 1977 (actual), FY 1978 (estimated), and FY 1979 (estimated) only.

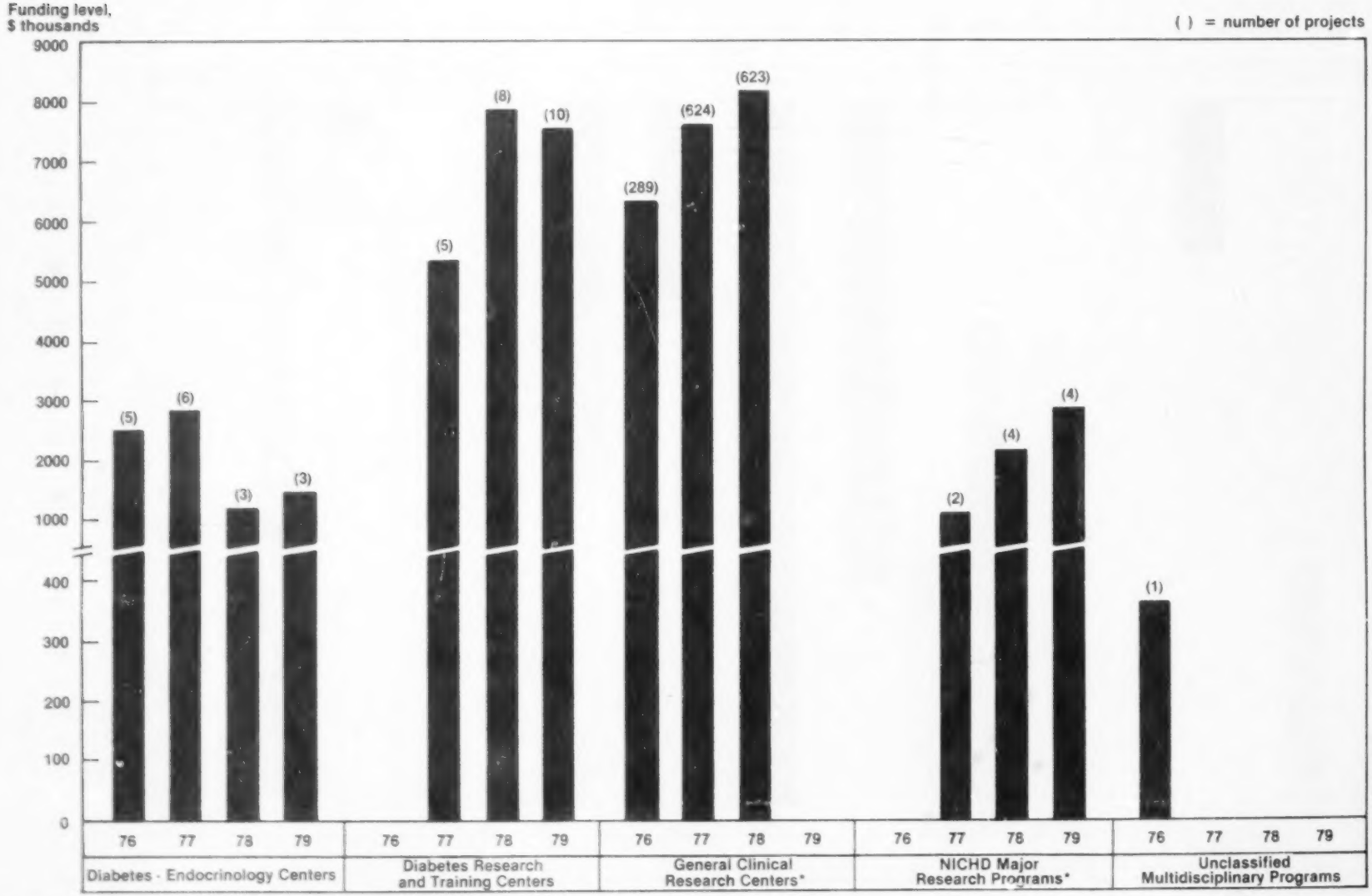
Health Care Delivery (C 1-8)



Manpower Development (D 1-3)

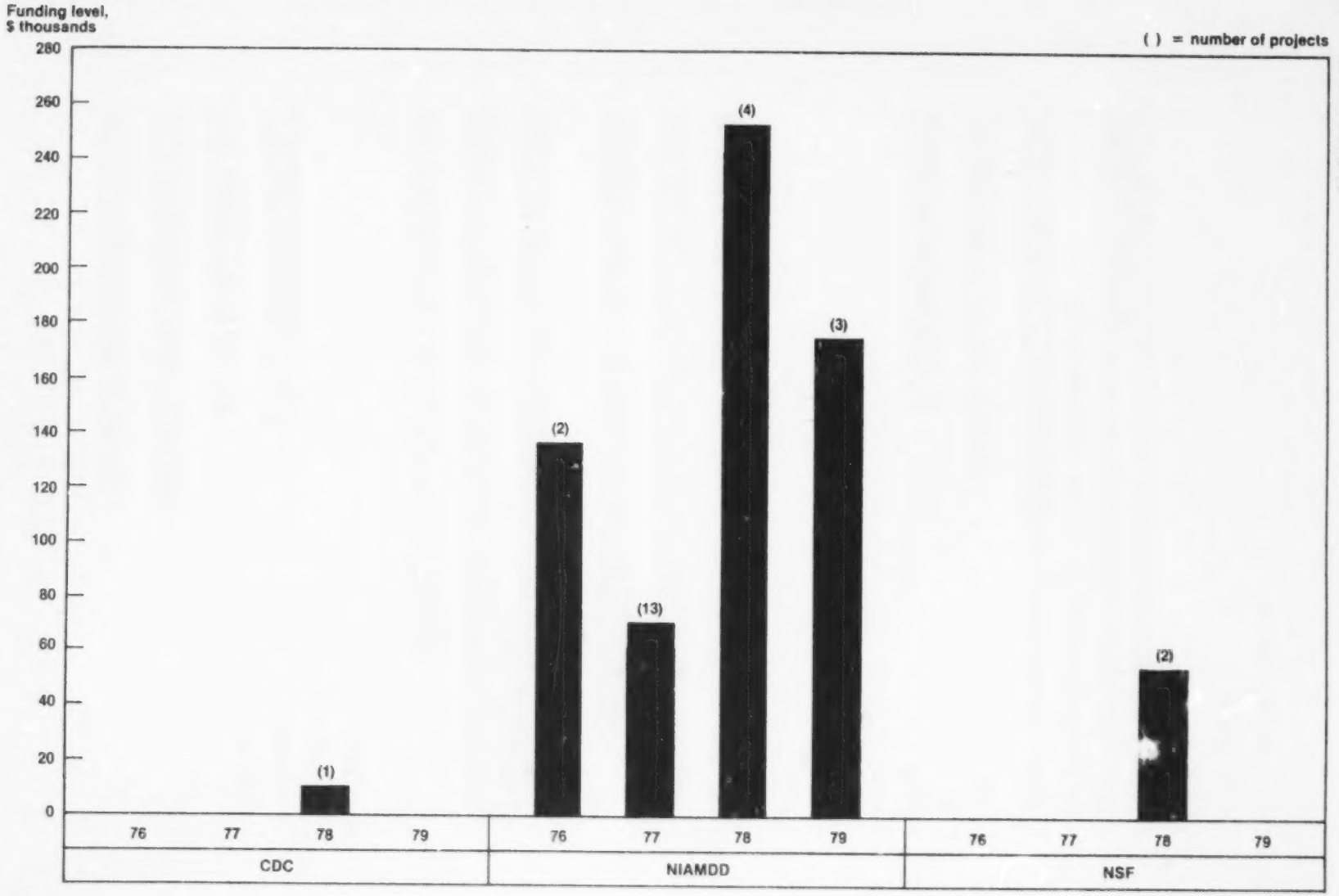


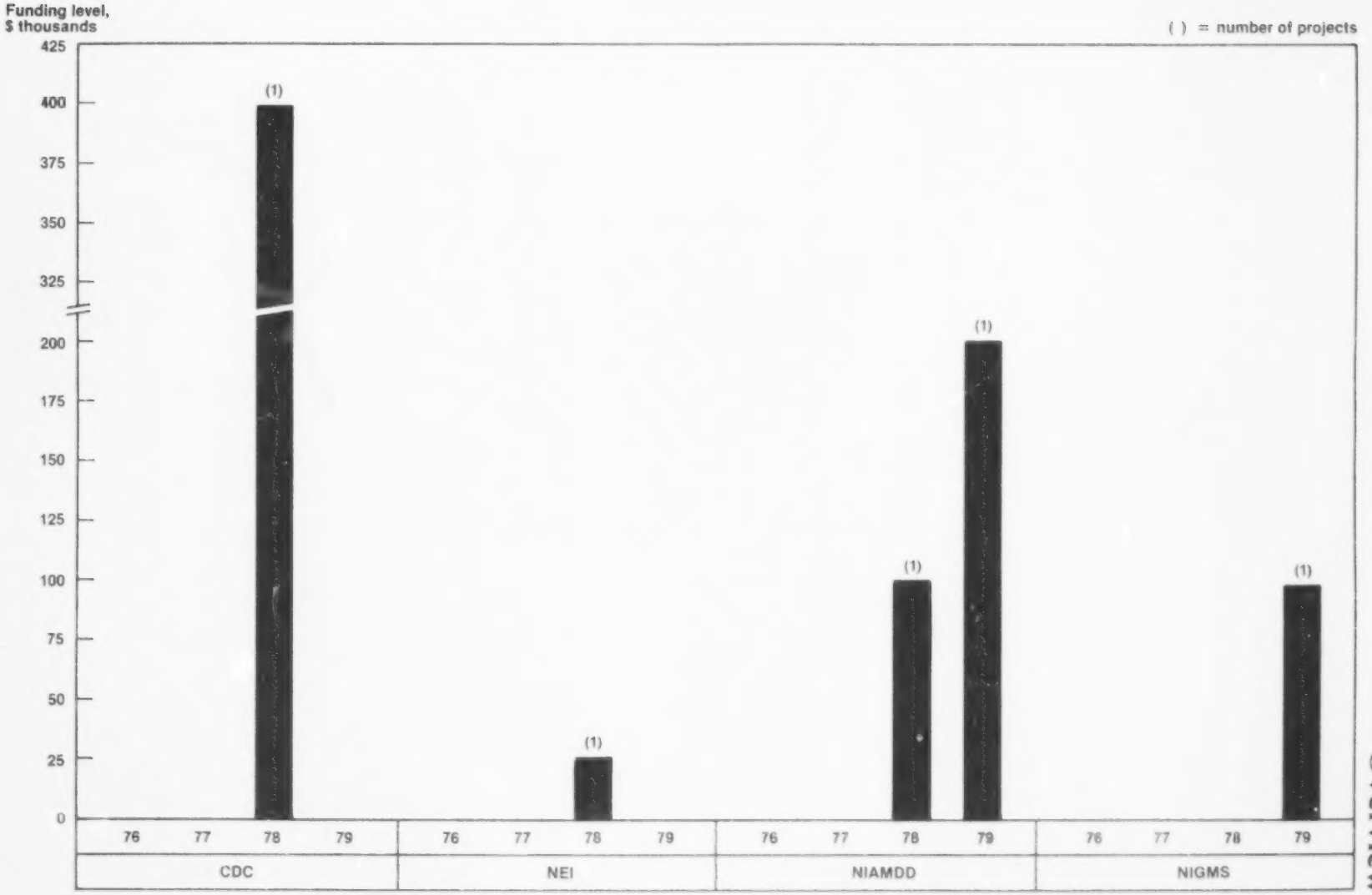
Multidisciplinary Programs (E 1-4)



*GCRC and NICHD projects and funds for FY 1977 and FY 1978 have been distributed and added into totals for appropriate subtopics in the "Research" category (B)

Workshops, Conferences, and Publications (F)




Funding level,
$ thousands
( ) = number of projects
425
400
375
350
325
200
175
150
125
100
75
50
25
0
(1)
(1)
(1)
(1)
(1)
76
77
78
79
CDC
NEI
NIAMDD
NIGMS

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